08/918407

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FILE 'USPAT' ENTERED AT 11:28:34 ON 09 MAR 1999

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*       WELCOME TO THE        *
*   U.S. PATENT TEXT FILE     *
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=> s p53

L1      1025 P53

=> s dna(w)(damage or damaged or damaging)

      30363 DNA
     296274 DAMAGE
     113500 DAMAGED
      69573 DAMAGING
L2      430 DNA(W)(DAMAGE OR DAMAGED OR DAMAGING)

=> s l1(10w)l2

L3       25 L1(10W)L2

=> t l3,cit,rel,ab,1-25
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1. 5,877,210, Mar. 2, 1999, Phosphotyrosine phosphatase inhibitors or phosphotyrosine kinase activators for controlling cellular proliferation; Gary L. Schieven, 514/492; 424/178.1, 179.1, 181.1; 435/184, 244; 556/1, 42, 44 [IMAGE AVAILABLE]

US PAT NO: 5,877,210 [IMAGE AVAILABLE] L3: 1 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 189,330, Jan. 31, 1994, Pat. No. 5,565,491.

ABSTRACT:
A method of inhibiting the proliferation of B cells by using inhibitors of phosphotyrosine phosphatase can be used to regulate the immune response and to treat diseases such as leukemias or lymphomas marked by malignant proliferation of B cells or T cells. Antitumor activity is seen in vivo against tumors and against tumor cell lines. The use of such inhibitors can be combined with radiation, which produces a synergistic effect. Several types of inhibitors can be used, including: (1) compounds comprising a metal coordinate-covalently bound to an organic moiety that can form a five- or six-membered ring, in which the metal is preferably vanadium (IV); (2) compounds in which vanadium (IV) is coordinate-covalently bound to an organic moiety such as a hydroxamate, .alpha.-hydroxypyridinone, .alpha.-hydroxypyrone, .alpha.-amino acid, hydroxycarbonyl, or thiohydroxamate; (3) coordinate-covalent complexes of vanadyl and cysteine or a derivative thereof; (4) nonhydrolyzable phosphotyrosine phosphatase analogues; (5) dephostatin; (6) 4-(fluoromethyl)phenyl phosphate and esterified derivatives; and (7) coordinate-covalent metal-organic compounds containing at least one oxo or peroxo ligand bound to the metal, in which the metal is preferably vanadium (V), molybdenum (VI), or tungsten (VI). Methods of stimulating signaling in T cells and conjugates of a modulator of phosphotyrosine metabolism with a specific binding partner for a B cell surface antigen are also disclosed.

2. 5,863,904, Jan. 26, 1999, Methods for treating cancers and restenosis with P21; Gary J. Nabel, et al., 514/44; 435/69.1, 375 [IMAGE AVAILABLE]

US PAT NO: 5,863,904 [IMAGE AVAILABLE] L3: 2 of 25

ABSTRACT:
The p21 gene encodes a cyclin dependent kinase inhibitor which affects cell cycle progression, but the role of this gene product in altering tumor growth has not been established. The present inventors have now discovered that the growth of malignant cells in vivo is inhibited by expression of p21. Expression of p21 resulted in an accumulation of cells in G.sub.0 /G.sub.1, alteration in morphology, and cell differentiation.

3. 5,863,795, Jan. 26, 1999, Nucleic acids that encode peptides which modulate apoptosis; Thomas D. Chittenden, et al., 435/325, 243, 320.1, 410; 536/23.5, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,863,795 [IMAGE AVAILABLE] L3: 3 of 25
REL-US-DATA: Division of Ser. No. 440,391, May 12, 1995, Pat. No. 5,656,725.

ABSTRACT:
The present invention is directed to novel peptides and compositions capable of modulating apoptosis in cells, and to methods of modulating apoptosis employing the novel peptides and compositions of the invention. In one aspect, the invention is directed to a novel peptide designated the "GD domain," which is essential both to Bak's interaction with Bcl-x.sub.L, and to Bak's cell killing function. Methods of identifying agonists or antagonists of GD domain function are provided. The GD domain is responsible for mediating key protein/protein interactions of significance to the actions of multiple cell death regulatory molecules.

4. 5,858,987, Jan. 12, 1999, E6AP antisense constructs and methods of use; Peggy L. Beer-Romero, et al., 514/44; 435/5, 6, 91.2; 536/23.1, 24.3, 24.33, 24.5 [IMAGE AVAILABLE]

US PAT NO: 5,858,987 [IMAGE AVAILABLE] L3: 4 of 25

ABSTRACT:
The present invention relates to the discovery that antisense nucleic acids complimentary to an E6AP gene can be used to regulate cellular p53 levels. In general the invention features E6AP antisense constructs which, by inhibiting E6AP activity, can modulate cellular p53 levels in both p53+ transformed cells and in normal cells. The invention also provides methods for treating papillomavirus (PV) induced condition, methods for regulating cellular p53 levels and methods for regulating cellular proliferation.

5. 5,858,678, Jan. 12, 1999, Apoptosis-regulating proteins; Govindaswamy Chinnadurai, 435/7.1, 365; 530/328, 329, 350; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,858,678 [IMAGE AVAILABLE] L3: 5 of 25
REL-US-DATA: Continuation of Ser. No. 284,139, Aug. 2, 1994, abandoned.

ABSTRACT:
Adenovirus E1B 19 kD protein protects against cell death induced by viral infection and certain external physical and chemical stimuli. Activity of the 19 kD protein is similar to the cell death suppressing activity of the protein coded by the Bcl-2 protooncogene. Bcl-2 protein can functionally substitute for the E1B 19 kD protein during adenovirus infection and in transformation of primary cells with adenovirus E1A. Five different cDNA's for proteins, designated Nip1, Nip2, Nip3, Bip1A and Bip13 that specifically interact with the 19 kD protein were found. Mutational analysis of the interaction indicates that at least four of the proteins (Nip1, Nip2, Nip3 and Bip1A) associate with 19 kD protein at specific sites thereof. Homologous motifs are found on Bcl2. An additional protein, (Bip5), interacts with Bcl-2 but not with the 19K protein.

6. 5,846,998, Dec. 8, 1998, Use of phosphotyrosine phosphatase inhibitors or phosphotyrosine kinase activators for controlling cellular proliferation; Gary L. Schieven, 514/492; 424/617, 646; 435/184, 326; 556/1, 42, 44 [IMAGE AVAILABLE]

US PAT NO: 5,846,998 [IMAGE AVAILABLE] L3: 6 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 189,330, Jan. 31, 1994, Pat. No. 5,565,491, Oct. 15, 1996.

ABSTRACT:

A method of inhibiting the proliferation of B cells by using inhibitors of phosphotyrosine phosphatase can be used to regulate the immune response and to treat diseases such as leukemias or lymphomas marked by malignant proliferation of B cells or T cells. Antitumor activity is seen in vivo against tumors and against tumor cell lines. The use o such inhibitors can be combined with radiation, which produces a synergistic effect. Several types of inhibitors can be used, including: (1) compounds comprising a metal coordinate-covalently bound to an organic moiety that can form a five- or six-membered ring, in which the metal is preferably vanadium (IV); (2) compounds in which vanadium (IV) is coordinate-covalently bound to an organic moiety such as a hydroxamate, .alpha.-hydroxypyridinone, .alpha.-hydroxypyrone, .alpha.-amino acid, hydroxycarbonyl, or thiohydroxamate; (3) coordinate-covalent complexes of cysteine or a derivative thereof; (4) nonhydrolyzable phosphotyrosine analogues; (5) dephostatin; (6) 4-(fluoromethyl)phenyl phosphate and esterified derivatives; and (7) coordinate-covalent metal-organic compounds containing at least one oxo or peroxo ligand bound to the

metal, in which the metal is preferably vanadium (V), molybdenum (VI), or tungsten (VI).

7. 5,843,737, Dec. 1, 1998, Cancer associated gene protein expressed therefrom and uses thereof; Lan Bo Chen, et al., 435/455, 6, 183, 320.1, 325, 477; 536/23.1, 23.2, 23.5 [IMAGE AVAILABLE]

US PAT NO: 5,843,737 [IMAGE AVAILABLE] L3: 7 of 25

ABSTRACT:
We have now discovered that eukaryotes, including mammals, have a gene that encodes a multifunctional protein having helicase activity, DNA repair activity, p53 sequestering activity and oncogenetic transformation potential. Enhanced transcripts and expression of this gene in non-testicular cells have a high correlation to disease state in a number of cancers, such as colorectal carcinomas, hereditary cancers resulting from defects in DNA repair pathways, breast cancers, etc. Accordingly, discovering enhanced levels of transcript or gene product in non-testicular tissues can be diagnostic of a predisposition to cancer, and prognostic for a particular cancer.

8. 5,843,684, Dec. 1, 1998, Method for detecting pre-cancerous or cancerous cells using P90 antibodies or probes; Arnold J. Levine, et al., 435/7.23, 6, 326; 436/64, 813; 530/387.7, 388.8, 388.85 [IMAGE AVAILABLE]

US PAT NO: 5,843,684 [IMAGE AVAILABLE] L3: 8 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 18,649, Feb. 17, 1993, abandoned, which is a continuation-in-part of Ser. No. 904,766, Jun. 26, 1992, abandoned, which is a continuation-in-part of Ser. No. 730,185, Jul. 12, 1991, abandoned, which is a continuation-in-part of Ser. No. 543,963, Jun. 27, 1990, abandoned.

ABSTRACT:

The invention provides a method of diagnosing cancer by determining the expression level or gene amplification of p53 and dm2, whereby an elevated level of either p53 or dm2 or both p53 and dm2 indicates a cancer diagnosis. Furthermore, the invention provides a method of predicting the progress of cancer by determining the expression level or gene amplification of p53 and dm2, whereby an elevated level of either p53 or dm2 or both p53 and dm2 indicated a poor prognosis.

9. 5,843,659, Dec. 1, 1998, Apoptosis gene EI24, compositions, and methods of use; Sophie M. Lehar, et al., 435/6, 69.1, 91.4, 320.1, 325; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,843,659 [IMAGE AVAILABLE] L3: 9 of 25

ABSTRACT:
Disclosed is the isolation and characterization of EI24, a novel gene whose 2.4 kb mRNA is induced following etoposide treatment. Induction of EI24 mRNA by etoposide required expression of wild-type p53. Overexpression of functional p53 was sufficient to induce expression of the EI24 mRNA. The EI24 mRNA was also induced in a p53-dependent manner
by ionizing irradiation of primary murine thymocytes. The invention is thus directed to an isolated EI24 protein, nucleotide sequences coding for and regulating expression of the protein, antibodies directed against the protein, and recombinant vectors and host cells containing the genetic sequences coding for and regulating the expression of the protein sequence. The invention is also directed to genomic DNA, cDNA, and RNA encoding the EI24 protein sequence and to corresponding antisense RNA sequences. Antibodies can be used to detect EI24 in biological specimens, including, for example, human tissue samples. The present invention is further directed to methods of treating degenerative disorders characterized in inappropriate cell proliferation or inappropriate cell death. The present invention is further directed to methods for diagnosing degenerative disorders characterized in inappropriate cell proliferation or inappropriate cell death, as well as methods for monitoring the progress of such degenerative disorders.

10. 5,840,579, Nov. 24, 1998, Nucleic acids encoding p53 mutations which suppress p53 cancer mutations; Jef D. Boeke, et al., 435/325, 254.2, 320.1; 536/23.1 [IMAGE AVAILABLE]

US PAT NO: 5,840,579 [IMAGE AVAILABLE] L3: 10 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 650,125, May 1, 1996.

ABSTRACT:
Intragenic suppressor mutations of common p53 mutations are able to function in cis and/or trans. These mutations are useful for identifying small molecule drugs which function in a similar fashion. In addition, the mutations themselves may be useful therapeutically, especially if they function in trans. Methods for rapidly obtaining this type of mutant employ a yeast selection system. Cells having both the negative mutation and intragenic suppressor are useful for studying the interactions of the two, in particular in determining the structure of the homotetramers and heterotetramers.

11. 5,834,487, Nov. 10, 1998, Inhibition of 26S and 20S proteasome by indanones; Robert T. Lum, et al., 514/319, 19, 561, 677 [IMAGE AVAILABLE]

US PAT NO: 5,834,487 [IMAGE AVAILABLE] L3: 11 of 25

ABSTRACT:
This invention is a method for inhibiting cell proliferation using indanones.

12. 5,830,751, Nov. 3, 1998, Genetic assays and strains using human TP53; Jef D. Boeke, et al., 435/254.2, 320.1; 536/23.1, 23.4 [IMAGE AVAILABLE]

US PAT NO: 5,830,751 [IMAGE AVAILABLE] L3: 12 of 25

ABSTRACT:
Yeast strains carrying a human wild-type TP53 are employed to select for mutations. The types of mutations can be analyzed genetically as recessive or dominant-negative. The mutational spectrum of dominant-negative TP53 mutants selected in yeast correlates tightly with TP53 mutations found in human cancers. Thus the use of such yeast assays is validated for studying the effects of various agents on human TP53, one of the most important and ubiquitous of human cancer genes. Assays, kits, and constructs are provide which use yeast as a genetic system for making and studying human TP53 mutations. Such assays can be used to develop therapeutic agents, to study putative carcinogens, and to identify other cellular components which interact with p53 and abrogate its activity.

13. 5,830,723, Nov. 3, 1998, Method for immortalizing chicken cells; Douglas N. Foster, et al., 435/467, 235.1, 325, 349, 373 [IMAGE AVAILABLE]

US PAT NO: 5,830,723 [IMAGE AVAILABLE] L3: 13 of 25

ABSTRACT:
This invention relates to the introduction of p53 under the control of the metallothionein promoter into primary cells to produce immortalized cell lines. The cells are useful as substrates for viral propagation, as contaminant-free sources for recombinant protein production, for recombinant virus production and as cell substrates to support primary cells and improve virus yield during virus propagation.

14. 5,780,454, Jul. 14, 1998, Boronic ester and acid compounds; Julian Adams, et al., 514/64; 544/229 [IMAGE AVAILABLE]

US PAT NO: 5,780,454 [IMAGE AVAILABLE] L3: 14 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 442,581, May 16, 1995, which is a continuation-in-part of Ser. No. 330,525, Oct. 28, 1994, abandoned.

ABSTRACT:
Disclosed herein is a method for reducing the rate of degradation of proteins in an animal comprising contacting cells of the animal with certain boronic ester and acid compounds. Also disclosed herein are novel boronic ester and acid compounds, their synthesis and uses.

15. 5,747,650, May 5, 1998, P53AS protein and antibody therefor; Molly F. Kulesz-Martin, 530/387.7, 387.1, 388.8, 389.1, 389.2 [IMAGE AVAILABLE]

US PAT NO: 5,747,650 [IMAGE AVAILABLE] L3: 15 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 100,496, Aug. 2, 1993.

ABSTRACT:
In accordance with the present invention, we have discovered and purified

a protein designated herein as p53as, which protein is present in normal cells of a mammal and is essentially identical to known normal growth controlling protein p53 of the same mammal, at least until the final 50 amino acids of the carboxy terminal end of the protein. The invention further includes an antibody specific for protein p53as, which antibody is designated herein as Ab p53as. The antibody may be either a monoclonal or polyclonal antibody and may be specific for p53as of any particular mammal such as mice and humans.

16. 5,747,469, May 5, 1998, Methods and compositions comprising DNA damaging agents and p53; Jack A. Roth, et al., 514/44; 435/320.1, 375; 514/2 [IMAGE AVAILABLE]

US PAT NO: 5,747,469 [IMAGE AVAILABLE] L3: 16 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 145,826, Oct. 29, 1993, which is a continuation-in-part of Ser. No. 960,513, Oct. 13, 1992, which is a continuation-in-part of Ser. No. 665,538, Mar. 6, 1991, abandoned.

ABSTRACT:
The present invention relates to the use of tumor suppressor genes in combination with a DNA damaging agent or factor for use in killing cells, and in particular cancerous cells. A tumor suppressor gene, p53, was delivered via a recombinant adenovirus-mediated gene transfer both in vitro and in vivo, in combination with a chemotherapeutic agent. Treated cells underwent apoptosis with specific DNA fragmentation. Direct injection of the p53-adenovirus construct into tumors subcutaneously, followed by intraperitoneal administration of a DNA damaging agent, cisplatin, induced massive apoptotic destruction of the tumors. The invention also provides for the clinical application of a regimen combining gene replacement using replication-deficient wild-type **p53** adenovirus and **DNA**-**damaging** drugs for treatment of human cancer.

17. 5,744,343, Apr. 28, 1998, Ubiquitin conjugating enzymes; Giulio Draetta, et al., 435/193, 252.3, 254.11, 320.1, 325; 536/23.2, 23.4 [IMAGE AVAILABLE]

US PAT NO: 5,744,343 [IMAGE AVAILABLE] L3: 17 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 247,904, May 23, 1994, which is a continuation-in-part of Ser. No. 176,937, Jan. 4, 1994, abandoned.

ABSTRACT:
The present invention concerns three ubiquitin-conjugating enzymes.

18. 5,726,025, Mar. 10, 1998, Assay and reagents for detecting inhibitors of ubiquitin-dependent degradation of cell cycle regulatory proteins; Marc W. Kirschner, et al., 435/7.2, 7.23, 7.7, 7.9, 15; 436/86, 503 [IMAGE AVAILABLE]

US PAT NO: 5,726,025 [IMAGE AVAILABLE] L3: 18 of 25

ABSTRACT:
The present invention provides a systematic and practical approach for the identification of candidate agents able to inhibit ubiquitin-mediated degradation of a cell-cycle regulatory protein, such as cyclins. One aspect of the present invention relates to a method for identifying an inhibitor of ubiquitin-mediated proteolysis of a cell-cycle regulatory protein by (i) providing a ubiquitin-conjugating system that includes the regulatory protein and ubiquitin under conditions which promote the ubiquitination of the target protein, and (ii) measuring the level of ubiquitination of the subject protein brought about by the system in the presence and absence of a candidate agent. A decrease in the level of ubiquitin conjugation is indicative of an inhibitory activity for the candidate agent. The level of ubiquitination of the regulatory protein can be measured by determining the actual concentration of protein:ubiquitin conjugates formed; or inferred by detecting some other quality of the subject protein affected by ubiquitination, including the proteolytic degradation of the protein.

19. 5,693,617, Dec. 2, 1997, Inhibitors of the 26s proteolytic complex and the 20s proteasome contained therein; Ross L. Stein, et al., 514/18, 19; 530/331; 560/20, 27, 31, 32, 41, 47, 159 [IMAGE AVAILABLE]

US PAT NO: 5,693,617 [IMAGE AVAILABLE] L3: 19 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 212,909, Mar. 15, 1994, abandoned.

ABSTRACT:
Disclosed herein is a method for reducing the rate of degradation of proteins in an animal comprising contacting cells of the animal with certain proteasome inhibitors. The structure of the inhibitors are also disclosed.

20. 5,672,686, Sep. 30, 1997, Bcl-Y - specific antibodies; Thomas D. Chittenden, 530/387.9, 388.2, 389.1, 391.3 [IMAGE AVAILABLE]

US PAT NO: 5,672,686 [IMAGE AVAILABLE] L3: 20 of 25
REL-US-DATA: Continuation-in-part of Ser. No. 287,427, Aug. 9, 1994, abandoned.

ABSTRACT:
The present invention is directed to an isolated Bcl-Y protein, nucleotide sequences coding for and regulating expression of the protein, antibodies directed against the protein, and recombinant vectors and host cells containing the genetic sequences coding for and regulating the expression of the protein sequence. The invention is also directed to genomic DNA, cDNA, and RNA encoding the Bcl-Y protein sequence and to corresponding antisense RNA sequences. Antibodies can be used to detect Bcl-Y in biological specimens, including, for example, human tissue samples. The present invention is further directed to methods of treating degenerative disorders characterized in inappropriate cell proliferation or inappropriate cell death. The present invention is further directed to methods for diagnosing degenerative disorders characterized in inappropriate cell proliferation or inappropriate cell death, as well as methods for monitoring the progress of such degenerative disorders.

21. 5,667,987, Sep. 16, 1997, P53 response genes; Leonard Buckbinder, et al., 435/69.1, 252.3, 254.11, 320.1; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,667,987 [IMAGE AVAILABLE] L3: 21 of 25

ABSTRACT:
Nucleic acid sequences, particularly DNA sequences, coding for all or part of p53 response protein PIGI-1, expression vectors containing the DNA sequences, host cells containing the expression vectors, and methods utilizing these materials are disclosed. The invention also concerns polypeptide molecules comprising all or part of p53 response protein PIGI-1, and methods for producing these polypeptide molecules.

22. 5,656,725, Aug. 12, 1997, Peptides and compositions which modulate apoptosis; Thomas D. Chittenden, et al., 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]

US PAT NO: 5,656,725 [IMAGE AVAILABLE] L3: 22 of 25

ABSTRACT:
The present invention is directed to novel peptides and compositions capable of modulating apoptosis in cells, and to methods of modulating apoptosis employing the novel peptides and compositions of the invention. In one aspect, the invention is directed to a novel peptide designated the "GD domain," which is essential both to Bak's interaction with Bcl-x.sub.L, and to Bak's cell killing function. Methods of identifying agonists or antagonists of GD domain function are provided. The GD domain is responsible for mediating key protein/protein interactions of significance to the actions of multiple cell death regulatory molecules.

23. 5,641,754, Jun. 24, 1997, Antisense oligonucleotide compositions for selectively killing cancer cells; Patrick L. Iversen, 514/44; 435/6, 91.1, 375; 536/23.1, 24.5 [IMAGE AVAILABLE]

US PAT NO: 5,641,754 [IMAGE AVAILABLE] L3: 23 of 25

ABSTRACT:
The present invention relates to methods and compositions for the treatment of cancer using an oligonucleotide and an hydroxyl radical up-regulator. The oligonucleotide is characterized by its ability to down-regulate the path by which the cell repairs oxidative damage to its DNA. Thus, the oligonucleotide renders the tumor cells more susceptible to eradication upon exposure to the hydroxyl radical up-regulator administered substantially concomitantly with or subsequent to administration of the oligonucleotide. This novel treatment, preferentially inhibits the proliferation or kills malignant cells but not normal cells. Preferably, the oligonucleotide is antisense to the gene which encodes protein p53, although other antisense oligonucleotides can also be used. The invention also includes novel conjugates of the oligonucleotide and the hydroxyl up-regulator, as well as new oligonucleotides.

24. 5,525,482, Jun. 11, 1996, Method and cell line for testing cytotoxicity and mutagenicity of a chemical; J. Christopher States, et al., 435/32, 29, 455 [IMAGE AVAILABLE]

US PAT NO: 5,525,482 [IMAGE AVAILABLE] L3: 24 of 25
REL-US-DATA: Continuation of Ser. No. 990,295, Dec. 9, 1992, abandoned, which is a continuation-in-part of Ser. No. 721,775, Jun. 27, 1991, Pat. No. 5,180,666.

ABSTRACT:
A method of testing the cytotoxicity and mutagenicity of a chemical includes the steps of exposing test cells to the chemical in vitro, intracellularly metabolizing the chemical into a mutagenic or cytotoxic metabolite and then detecting gene/protein/cell damage in the test cells as an indication of the mutagenicity/cytotoxicity of the chemical.
A cell line is provided for testing cytotoxicity and mutagenicity of the chemicals, the cell line consisting essentially of fibroblasts normally having no detectable cytochrome P450 mixed function oxidase enzyme activity. The fibroblasts are transformed with chimeric gene constructs containing cytochrome P450 coding sequences and have intracellular cytochrome P450 oxidative metabolizing activity.

25. 5,180,666, Jan. 19, 1993, Method and cell line for testing mutagenicity of a chemical; J. Christopher States, et al., 435/29, 366, 455 [IMAGE AVAILABLE]

US PAT NO: 5,180,666 [IMAGE AVAILABLE] L3: 25 of 25

ABSTRACT:
A method of testing the mutagenicity of a chemical includes the steps of exposing test cells to the chemical in vitro, intracellularly metabolizing the chemical into a mutagenic or cytotoxic metabolite and then detecting gene/protein/cell damage in the test cells as an indication of the mutagenicity/cytotoxicity of the chemical.
A cell line is provided for testing mutagenicity of the chemicals, the cell line consisting essentially of fibroblasts normally having no detectable cytochrome P450 mixed function oxidase enzyme activity. The fibroblasts are transformed with chimeric gene constructs containing cytochrome P450 coding sequences and have intracellular cytochrome P450 oxidative metaboli zing activity.

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? s dna or plasmid or vector

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Processing
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   S2 1968623  DNA OR PLASMID? OR VECTOR?
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Processing
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? s s4 and s3

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   S5    617  S4 AND S3
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Processing
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KILLER OR KILLS
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? rd

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
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...examined 50 records  (100)
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...examined 50 records  (300)
...completed examining records
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Processing
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   S10    16  S9 AND PY<=1994
? t s10/3,ab/1-16


 10/3,AB/1    (Item 1 from file: 5)
DIALOG(R)File  5:BIOSIS PREVIEWS(R)
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09670396  BIOSIS NO.: 199598125314
Filtered, tar- and aerosol-free cigarette smoke causes accumulation of the
 tumor suppressor protein p53 in rodent cells.

AUTHOR: Schulze-Lutum Annegret; Siegel Johanna; Schmidt Ralf J;
Plaumann
 Bettina; Braun Christine; Haessler Christel; Brandner Gerhard; Hess Ralf
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JOURNAL: International Journal of Oncology  5 (6):p1405-1409 1994
ISSN: 1019-6439
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cigarette smoke was filtered with a Cambridge glass fiber filter
 retaining 99.9% of the tar and aerosol fraction and diluted 1:5 with air.
 The murine cell line L929 was exposed to this smoke preparation for
 periods of up to 10 min. Thereafter the following parameters were
 determined at different times: Nuclear accumulation of the tumor
 suppressor protein p53 indicating chromatin injury (by immunostaining);
 apoptotic DNA fragmentation (by DNA end labelling with biotin-16-dUTP in
 the presence of terminal deoxyribonucleotidyl transferase); the
 intracellular level of reactive oxygen intermediates (ROI) (by
 cytofluorimetry with the fluorigenic stain 2',7'-dichlorofluorescin
 diacetate). After 1 min exposure to 1:5 air-diluted filtered cigarette
 smoke maximal %%%p53%%% accumulation occurred about 20 h later,
whereas
 maximal %%%DNA%%% fragmentation and %%%apoptosis%%% and
maximal ROI
 levels were found after 10 min of exposure. Obviously, even the diluted,
 tar- and aerosol-free fraction of cigarette smoke has the potency, after
 1 min of exposure only, to exert severe DNA damage, a potential
 transformation risk for the surviving cell fraction, in murine cell
 cultures as indicated by stabilization and accumulation of the tumor
 suppressor protein p53.


 10/3,AB/2    (Item 2 from file: 5)
DIALOG(R)File  5:BIOSIS PREVIEWS(R)
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09589724  BIOSIS NO.: 199598044642
P53 expression in nitric oxide-induced apoptosis.

AUTHOR: Messmer Udo K; Ankarcrona Maria; Nicotera Pierluigi; Bruene
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78434
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JOURNAL: FEBS Letters  355 (1):p23-26 1994
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Nitric oxide (NO) is a diffusible messenger involved in several
 patho-physiological processes including immune-mediated cytotoxicity and
 neural cell killing. NO or the products of its redox chemistry can cause
 DNA damage and activate subsequent lethal reactions including energy
 depletion and cell necrosis. However, regardless of whether it is
 endogenously produced in response to cytokines, or generated by chemical
 breakdown of donor molecules, NO can also induce apoptosis in different
 systems. Here, we report that NO generation in response to a cytokine
 induced NO-synthase or by NO donors stimulates the expression of the
 tumor suppressor gene, p53, in RAW 264.7 macrophages or pancreatic
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RINm5F
cells prior to apoptosis. NO-synthase inhibitors such as N-G-monomethyl-L-arginine prevent the inducible NO generation as well as p53 expression and apoptosis. Since %%%p53%%% expression is linked to %%%apoptosis%%% in some cells exposed to %%%DNA%%% damaging agents, we
suggest that NO-induced %%%apoptosis%%% in these cell systems is the consequence of DNA damage and subsequent expression of this tumor suppressor gene.

10/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09582354 BIOSIS NO.: 199598037272
P53 gene mutations are associated with decreased sensitivity of human lymphoma cells to DNA damaging agents.

AUTHOR: Fan Saijun; El-Deiry Wafik S; Bae Insoo; Freeman Jim; Jondle Daniel
; Bhatia Kishor; Fornace Albert J Jr; Magrath Ian; Kohn Kurt W; O'Connor Patrick M(a)
AUTHOR ADDRESS: (a)Lab. Molecular Pharmacol., Developmental Therapeutics
Program, Div. Cancer Treatment, National C, USA

JOURNAL: Cancer Research 54 (22):p5824-5830 1994
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The present study assessed the role of the p53 tumor suppressor gene in cell cycle arrest and apoptosis following treatment of Burkitt's lymphoma and lymphoblastoid cell fines with gamma-rays, etoposide, nitrogen mustard, and cisplatin. Cell cycle arrest was measured by flow cytometry; p53 and p21-Waf1/Cip1 protein levels were measured by Western blotting; cell survival was measured in 72-96-h growth inhibition assays and by trypan blue staining, and apoptotic DNA fragmentation was assessed by either agarose gel electrophoresis or a modified filter elution method. We found that gamma-rays and etoposide induced a strong G-1 arrest in the wild-type p53 lines while nitrogen mustard and cisplatin induced relatively little G-1 arrest. All agents failed to induce G-1 arrest in cells containing mutant p53 genes. The degree of G-1 arrest observed with these agents correlated with the rate of p53 and p21 protein accumulation: gamma-rays and etoposide induced rapid accumulation of both p53 and p21-Waf1/Cip1 nitrogen mustard and cisplatin induced slow accumulation of p53 and no major accumulation of the p21-Waf1/Cip1 protein. Despite differences in G-1 arrest and kinetics of p53 or p21-Waf1/Cip1 protein accumulation, all agents tended to decrease survival to a greater extent in the wild-type p53 lines compared to the mutant p53 lines. Cell death in the wild-type %%%p53%%% lines was associated with intracellular %%%DNA%%% degradation into oligonucleosomal
sized %%%DNA%%% fragments, indicative of %%%apoptosis%%%. We also
observed an inverse sensitivity relationship between nitrogen mustard/cisplatin and etoposide in the mutant p53 lines and this was found to correlate with topoisomerase 11 mRNA levels in the cells. Our results suggest that p53 gene status is an important determinant of both radio- and chemosensitivity in lymphoid cell lines and that p53 mutations are often associated with decreased sensitivity to DNA damaging agents.

10/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09412878 BIOSIS NO.: 199497421248
The selenium metabolite selenodiglutathione induces p53 and apoptosis: Relevance to the chemopreventive effects of selenium?

AUTHOR: Lanfear Jerry; Fleming Janis; Wu Leonard; Webster Gill; Harrison Paul R(a)
AUTHOR ADDRESS: (a)Beatson Inst. Cancer Res., Cancer Res. Campaign Beatson
Lab., Garscube Estate, Switchback Road, , UK

JOURNAL: Carcinogenesis (Oxford) 15 (7):p1387-1392 1994
ISSN: 0143-3334
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Selenodiglutathione (SDG), the initial metabolite of selenite, is shown to be a more powerful inhibitor of cell growth in vitro than selenite itself. This has been established both with mouse erythroleukaemia (MEL) cells and an ovarian cell line (A2780) which is known to contain wild-type p53. Other seleno-compounds, such as selenomethyl selenocysteine (SMS) and dimethyl selenoxide (DMS), which are potent chemopreventive agents and are known to be metabolized to methylated selenium derivatives directly rather than via SDG, are also growth inhibitory to both MEL and A2780 cells, although less so than SDG or selenite. However, cells growth-inhibited by DMS are more viable than cells growth-inhibited to the same extent by SDG or selenite, suggesting that the methylated seleno-compounds may inhibit cell growth in a different manner from that of SDG or selenite. Our studies of the mechanism of growth inhibition by SDG, have established two facts. First, SDG induces p53 protein levels in cells that contain wild-type %%%p53%%%
(A2780 cells), suggesting that SDG induces the %%%DNA%%% damage-recognition pathway. Secondly, SDG induces %%%apoptosis%%% in MEL
cells, as judged by flow cytometry and formation of nucleosomal DNA ladders. However, since p53 mutations have been found to be targetted events in all MEL cells examined, our evidence suggests that induction of apoptosis by SDG is not absolutely dependent on the p53 response pathway.

10/3,AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09406991 BIOSIS NO.: 199497415361
P53-dependent apoptosis in the absence of transcriptional activation of p53-target genes.

AUTHOR: Caelles Carme(a); Helmberg Arno; Karin Michael
AUTHOR ADDRESS: (a)Inst. Invest. Biomed., Arturo Duperier 4, 28029-Madrid,
Spain

JOURNAL: Nature (London) 370 (6486):p220-223 1994
ISSN: 0028-0836
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The tumour suppressor p53 is required to induce programmed cell
death (apoptosis) by DNA-damaging agents. As p53 is a transcriptional activator that mediates gene induction after DNA damage, it has been proposed to be a genetic switch that activates apoptosis-mediator genes. Here we evaluate the role of %%%p53%%% in
%%%DNA%%%-damage-induced
%%%apoptosis%%% by establishing derivatives of GHFT1 cells, that are somatotropic progenitors immortalized by expression of SV40 T-antigen, which express a temperature-sensitive p53 mutant. In these cells induction of apoptosis by DNA damage depends strictly on p53 function. A shift to the permissive temperature triggers apoptosis following DNA damage, but this is independent of new RNA or protein synthesis. The extent of apoptotic DNA cleavage is directly proportional to the period during which p53 is functional. These results do not support the proposal that p53 is an activator of apoptosis-mediator genes but rather indicate that p53 either represses genes necessary for cell survival or is a component of the enzymatic machinery for apoptotic cleavage or repair of DNA.

10/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09300275 BIOSIS NO.: 199497308645
Apoptosis in erythroid progenitors deprived of erythropoietin occurs during the G-1 and S phases of the cell cycle without growth arrest or stabilization of wild-type p53.

AUTHOR: Kelley Linda L(a); Green Wayne F; Hicks Geoffrey G; Bondurant Maurice C; Koury Mark J; Ruley H Earl
AUTHOR ADDRESS: (a)Dep. Pathol., University Utah Sch. Med., 50 North Medical Dr., Salt Lake City, UT 84132, USA

JOURNAL: Molecular and Cellular Biology 14 (6):p4183-4192 1994
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

QH506. M6
Film

ABSTRACT: Erythropoietin (Epo) inhibits apoptosis in murine proerythroblasts infected with the anemia-inducing strain of Friend virus (FVA cells). We have shown that the apoptotic process in FVA cell populations deprived of Epo is asynchronous as a result of a heterogeneity in Epo dependence among individual cells. Here we investigated whether apoptosis in FVA cells correlated with cell cycle phase or stabilization of p53 tumor suppressor protein. DNA analysis in nonapoptotic FVA cell subpopulations cultured without Epo demonstrated little change in the percentages of cells in G-1, S, and G-2/M phases over time. Analysis of the apoptotic subpopulation revealed high percentages of cells in G-1 and S, with few cells in G-2/M at any time. When cells were sorted from G-1 and S phases prior to culture without Epo, apoptotic cells appeared at the same rate in both populations, indicating that no prior commitment step had occurred in either G-1 or S phase. Steady-state wild-type p53 protein levels were very low in FVA cells compared with control cell lines and did not accumulate in Epo-deprived cultures; however, %%%p53%%% protein did accumulate when FVA cells were treated with the %%%DNA%%%-damaging agent actinomycin D. These data indicate that erythroblast %%%apoptosis%%% caused by Epo deprivation (i) occurs throughout G-1 and S phases and does not require cell cycle arrest, (ii) does not have a commitment event related to cell cycle phase, and (iii) is not associated with conformational changes or stabilization of wild-type p53 protein.

10/3,AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09039274 BIOSIS NO.: 199497047644
Wild-type p53-triggered apoptosis is inhibited by bcl-2 in a v-myc-induced T-cell lymphoma line.

AUTHOR: Wang Yisong(a); Szekely Laszlo; Okan Ismail; Klein George; Wiman Klas G
AUTHOR ADDRESS: (a)Dep. Tumor Biology, Karolinska Inst., Box 60400, S-10401 Stockholm, Sweden

JOURNAL: Oncogene 8 (12):p3427-3431 1993
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

RC268.42.048

ABSTRACT: Using a temperature sensitive p53 construct (ts p53), we have earlier shown that expression of wild-type (wt) p53 triggers apoptosis in a v-myc-induced T-cell lymphoma line that lacks endogenous p53, and in a Burkitt lymphoma line that carries mutant p53. We have suggested that apoptosis is elicited by the contradictory signals emanating from the constitutively activated myc gene and the growth arresting signal of wt p53 (Ramqvist et al., 1993; Wang et al., 1993). Work in other laboratories has shown that constitutive c-myc expression can induce apoptosis when cell proliferation is inhibited due to the lack of growth stimulating factors. Expression of bcl-2 could inhibit apoptosis. In order to test whether p53-induced apoptosis can be prevented by bcl-2, we have introduced a retrovirally driven bcl-2 construct into our v-myc-induced murine T-cell lymphoma line, previously transfected with ts p53. About 90% of the parental ts p53 transfected cells died of apoptosis within 3 days after induction of wt p53 expression at 32 degree C. Two clones of ts p53/bcl-2 double transfectants that expressed high levels of bcl-2 from the introduced construct were completely protected from apoptosis, following transfer of the cells to 32 degree C. One clone that expressed the exogenous bcl-2 only at a low level was partially protected from wt p53-induced apoptosis. Clones of the parental ts %%%p53%%% carrying cells transfected with the puromycin resistance gene %%%vector%%%, without the bcl-2 gene underwent 90% %%%apoptosis%%%. These results suggest that bcl-2 may prevent apoptosis in cells simultaneously exposed to the proliferation-stimulating effect of activated myc and the growth arresting signal of wt p53.

10/3,AB/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08962956 BIOSIS NO.: 199396114457
A retroviral wild-type %%%p53%%% expression %%%vector%%% penetrates human lung cancer spheroids and inhibits growth by inducing %%%apoptosis%%%.

AUTHOR: Fujiwara Toshiyoshi; Grimm Elizabeth A; Mukhopadhyay Tapas; Cai De Wei; Owen-Schaub Laurie B; Roth Jack A(a)
AUTHOR ADDRESS: (a)Dep. Thoracic Cardiovascular Surg., Univ. Texas M.D. Anderson Cancer Center, Houston, TX 77030, USA

JOURNAL: Cancer Research 53 (18):p4129-4133 1993
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

RC261. A1C15
Film

ABSTRACT: Multicellular tumor spheroids approximate the three-dimensional configuration of primary and metastatic tumors. The effects of retrovirus-mediated transduction of wild-type p53 (wt-p53) were studied on multicellular tumor spheroids of human non-small cell lung cancer cell lines H322a, the p53 gene of which is homozygously mutated at codon 248, and WT226b, which has endogenous wt-p53. The growth of WT226b spheroids was not affected by exogenous wt-p53 transduction; the growth of H322a spheroids, however, was significantly inhibited by the addition of wt-p53 virus stocks. Transduction of cells by the wt-p53 retroviral vector and penetration of multiple cell layers in H322a spheroids was demonstrated by in situ polymerase chain reaction/hybridization with the neomycin-resistant neo probe. Apoptotic changes indicating programmed cell death were observed in H322a spheroids treated with the wt-p53 virus. These results suggest that retroviral vectors can penetrate into multiple cell layers of three-dimensional tumor masses and induce potentially therapeutic effects.

10/3,AB/9 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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05753425 EMBASE No: 1994161701
Apoptosis in erythroid progenitors deprived of erythropoietin occurs during the Ginf 1 and S phases of the cell cycle without growth arrest or stabilization of wild-type p53
Kelley L.L.; Green W.F.; Hicks G.G.; Bondurant M.C.; Koury M.J.; Ruley H.E.
Department of Pathology, Utah University School of Medicine, 50 North Medical Dr.,Salt Lake City, UT 84132 United States
Molecular and Cellular Biology (MOL. CELL. BIOL.) (United States) 1994 , 14/6 (4183-4192)

CODEN: MCEBD ISSN: 0270-7306
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Erythropoietin (Epo) inhibits apoptosis in murine proerythroblasts infected with the anemia-inducing strain of Friend virus (FVA cells). We have shown that the apoptotic process in FVA cell populations deprived of Epo is asynchronous as a result of a heterogeneity in Epo dependence among individual cells. Here we investigated whether apoptosis in FVA cells correlated with cell cycle phase or stabilization of p53 tumor suppressor protein. DNA analysis in nonapoptotic FVA cell subpopulations cultured without Epo demonstrated little change in the percentages of cells in Ginf 1, S, and Ginf 2/M phases over time. Analysis of the apoptotic

subpopulation revealed high percentages of cells in Ginf 1 and S, with few cells in Ginf 2/M at any time. When cells were sorted from Ginf 1 and S phases prior to culture without Epo, apoptotic cells appeared at the same rate in both populations, indicating that no prior commitment step had occurred in either Ginf 1 or S phase. Steady- state wild-type p53 protein levels were very low in FVA cells compared with control cell lines and did not accumulate in Epo-deprived cultures; however, %%%p53%%% protein did accumulate when FVA cells were treated with the %%%DNA%%%-damaging agent
actinomycin D. These data indicate that erythroblast %%%apoptosis%%% caused
by Epo deprivation (i) occurs throughout Ginf 1 and S phases and does not require cell cycle arrest, (ii) does not have a commitment event related to cell cycle phase, and (iii) is not associated with conformational changes or stabilization of wild-type p53 protein.

10/3,AB/10 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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05654838 EMBASE No: 1994070095
Tumor suppressor genes
Hinds P.W.; Weinberg R.A.
Harvard Medical School, Department of Pathology-D2333, 200 Longwood Avenue,Boston, MA 02115 United States
Current Opinion in Genetics and Development (CURR. OPIN. GENET. DEV.) (
United Kingdom) 1994, 4/1 (135-141)

CODEN: COGDE ISSN: 0959-437X
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The mutation of tumor suppressor genes is thought to contribute to tumor growth by inactivating proteins that normally act to limit cell proliferation. Several tumor suppressor proteins have been identified in recent years, but only two of them, p53 and pRb, are understood in detail. In the past year, a role has become apparent for both of these proteins in transcription and phosphorylation events required for passage of a cell from G1 to S phase. The pRb protein appears to prevent the function of transcription factors and other proteins needed for S phase until its inactivation by cyclin-dependent kinases in late G1. Induction of %%%p53%%%
by %%%DNA%%% damage may act to cause cell cycle arrest or %%%cell%%%
%%%death%%% by altering the transcription program of damaged cells. A detailed molecular understanding of these growth regulators is now emerging, and is the subject of this review.

10/3,AB/11 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
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05305661 EMBASE No: 1993073746
Induction of nuclear accumulation of the tumor-suppressor protein p53 by DNA-damaging agents
Fritsche M.; Haessler C.; Brandner G.
Abteilung Virologie, Inst fur Medizinische Mikrobiologie/, Hygiene der Universitat, POB 820,D 78 Freiburg Germany
Oncogene (ONCOGENE) (United Kingdom) 1993, 8/2 (307-318)

CODEN: ONCNE ISSN: 0950-9232
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Cancer therapy drugs, such as diamminedichloroplatinum (cisplatin), mitomycin C, etoposide and a number of other compounds, as well as energy-rich radiation, are known to act on cellular DNA. These agents are shown to induce nuclear accumulation of the so-called tumor-suppressor protein p53 in fibroblastoid cells, as well as in epithelioid normal and immortalized cells of murine, simian, and human origin. p53 accumulation starts a few hours after treatment and can remain detectable in surviving cells for at least 20 days. Accumulation occurs because of increased p53 protein stability and depends on ongoing translation. It is not the result of enhanced gene expression. A number of cell cycle inhibitors do not affect p53 protein accumulation, suggesting that the process may start from several points in the cell cycle. Since the increase in the nuclear p53 protein levels occurs within a few hours in most of the treated normal diploid cells, it is unlikely that the accumulated p53 protein is derived from a mutated p53 gene. The results obtained are in accordance with the view that the DNA damage-induced %%%p53%%% accumulation may either inhibit
cell growth, allowing %%%DNA%%% repair processes, or, in the case of severe
damage, initiate %%%apoptosis%%%.

10/3,AB/12 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0174148 DBA Accession No.: 95-00969
An oligonucleotide complementary to %%%p53%%% mRNA acts synergistically
with oxidant stress and %%%DNA%%% damage to stimulate %%%apoptosis%%%
in acute myeloid leukemia - tumor suppressor antisense oligonucleotide characterization (conference abstract)
AUTHOR: Bayever E; Copple B L; Haines K M; Iversen P L
CORPORATE AFFILIATE: Univ.Nebraska
CORPORATE SOURCE: Department of Pediatrics, University of Nebraska Medical
Center, Omaha, Nebraska 68198, USA.
JOURNAL: Cancer Gene Ther. (1, 4, 330) %%%1994%%%
CODEN: 2815V
CONFERENCE PROCEEDINGS: Gene Therapy of Cancer, 3rd International Conference, San Diego, CA, 10-12 November, 1994.
LANGUAGE: English
ABSTRACT: An oligonucleotide complementary to p53 mRNA showed a cytotoxic
effect on human myeloid leukemia blasts in vitro. To elucidate the mechanism of action further and enhance the in vivo efficacy of the oligonucleotide, the role of oxidative stress and DNA damage was investigated. Using human acute myeloid leukemia (AML) cell lines and primary human AML cells, the cytotoxic effect of the oligonucleotide was enhanced by addition of hydrogen peroxide or mitoxantrone, and abrogated by ascorbic acid. Cells cultured in a low oxygen environment, which more closely mimicked in vivo oxygen content, did not respond to the oligonucleotide unless hydrogen peroxide or mitoxantrone were added. Suppression of p53 protein and mRNA was noted by Western blot and reverse transcription-polymerase chain reaction, indicating that part of the mechanism was due to an antisense effect. These findings provide the basis for designing effective clinical trials. (0 ref)

10/3,AB/13 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0171580 DBA Accession No.: 94-14131
Tumor suppressor gene therapy of cancer: adeno viral mediated gene transfer of p53 and retinoblastoma cDNA into human tumor cell lines - potential cancer gene therapy using an adeno virus vector (conference abstract)
AUTHOR: Wills K N; Maneval D C; Menzel P; Sutjipto S; Wen S F; Nared-Hood K
CORPORATE AFFILIATE: Canji
CORPORATE SOURCE: Canji Inc., 3030 Science Park Road, San Diego, CA 92121,
USA.
JOURNAL: J.Cell.Biochem. (Suppl.18C, 204) %%%1994%%%
CODEN: JCEBD5
LANGUAGE: English
ABSTRACT: Mutations or loss of the p53 and/or retinoblastoma (Rb) tumor suppressor genes are associated with a vast array of human malignancies. Reintroduction of wild-type p53 or Rb into these deficient tumor cells has been shown to suppress their tumorigenic properties, and in some cases induce apoptosis. Therefore, p53 and Rb gene therapy may be a viable means of treating many types of cancer. A series of adeno virus vectors which directed the expression of either wild-type p53 or Rb was constructed. These vectors were deleted for the adeno viral E1a and E1b genes required for viral replication, and these regions were replaced with expression DNA cassettes containing tumor suppressor genes driven by the adeno virus-2 major late promoter or the cytomegalo virus promoter. An additional construct with the Rb gene driven by its own promoter was also constructed. In p53 or Rb null/mutant tumor cell lines infected with these viruses, %%%p53%%% or

Rb was expressed, %%%DNA%%% replication was suppressed, cell growth was
affected and %%%apoptosis%%% was induced in some cases. Cancer gene
therapy is currently being tested in animal models. (0 ref)

10/3,AB/14 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0170916 DBA Accession No.: 94-13467
Tumor suppressor gene therapy of cancer: adeno viral mediated gene transfer of the p53 gene into human tumor cell lines - adeno virus vector-mediated expression in tumor cell culture for potential cancer gene therapy (conference abstract)
AUTHOR: Gregory R J; Maneval D C; Sutjipto S; Wen S F; Harris M P; Nared-Hood K
CORPORATE AFFILIATE: Canji
CORPORATE SOURCE: Canji Inc., 3030 Science Park Road, San Diego, CA 92121,
USA.
JOURNAL: J.Cell.Biochem. (Suppl.18A, 237) %%%1994%%%
CODEN: JCEBD5
LANGUAGE: English
ABSTRACT: Introduction of wild-type p53 tumor suppressor into p53 altered human tumor cells suppresses their tumorigenic properties and, in some cases, induces apoptosis. In principle, p53 gene therapy would seem suitable for many forms of tumor. A series of adeno virus vectors which directed expression of the human wild-type p53 gene were constructed. The vectors were deleted for adeno viral E1a and E1b genes required for viral replication and had substitutions in their place of the p53 gene under the control of the adeno virus major late promoter of cytomegalo virus. Infection of p53null or p53mut tumor cell lines with these viruses (or appropriate controls) indicated that they could express %%%p53%%%, suppress %%%DNA%%% replication, inhibit cell growth and
induce %%%apoptosis%%% in certain cell lines. Other human tumor cells appeared to be refractory to these effects. Interestingly, preliminary evidence suggested that the cells which did not respond to the p53 adeno viruses may not be efficiently infected by Ad5-based vectors. These results suggested that adeno virus-mediated p53 gene transfer may be effective for cancer gene therapy. (0 ref)

10/3,AB/15 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

122006893 CA: 122(1)6893c JOURNAL
DNA damage can induce apoptosis in proliferating lymphoid cells via p53-independent mechanisms inhibitable by Bcl-2
AUTHOR(S): Strasser, Andreas; Harris, Alan W.; Jacks, Tyler; Cory, Suzanne
LOCATION: Walter and Eliza Hall Institue of Med. Res., Royal Melbourne Hospital, 3050, Victoria, Austria
JOURNAL: Cell (Cambridge, Mass.) DATE: 1994 VOLUME: 79 NUMBER: 2
PAGES: 329-39 CODEN: CELLB5 ISSN: 0092-8674 LANGUAGE: English

10/3,AB/16 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

120160322 CA: 120(13)160322f JOURNAL
The role of p53 in spontaneous and radiation-induced apoptosis in the gastrointestinal tract of normal and p53-deficient mice
AUTHOR(S): Merritt, Anita J.; Potten, Christopher S.; Kemp, Christopher J.; Hickman, John A.; Balmain, Allan; Lane, David P.; Hall, Peter A.
LOCATION: Paterson Inst Cancer Res., Christie Hosp. (NHS), Manchester, UK, M20 9BX
JOURNAL: Cancer Res. DATE: 1994 VOLUME: 54 NUMBER: 3 PAGES: 614-17
CODEN: CNREA8 ISSN: 0008-5472 LANGUAGE: English
? s dna(w)(damage or damaged or damaging)

1683048 DNA
616350 DAMAGE
85912 DAMAGED
41857 DAMAGING
S11 52211 DNA(W)(DAMAGE OR DAMAGED OR DAMAGING)
? s s1(10w)s11

50800 S1
52211 S11
S12 1336 S1(10W)S11
? rd

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14/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09440127 BIOSIS NO.: 199497448497
Mice with DNA repair gene (ERCC-1) deficiency have elevated levels of p53, liver nuclear abnormalities and die before weaning.

AUTHOR: McWhir Jim; Selfridge Jim; Harrison David J; Squires Shoshana; Melton David W(a)
AUTHOR ADDRESS: (a)Inst. Cell and Molecular Biol., Univ. Edinburgh, Mayfield Road, Edinburgh EH9 3JR, UK

JOURNAL: Nature Genetics 5 (3):p217-224 1993
ISSN: 1061-4036
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Defects in nucleotide excision repair are associated with the human condition xeroderma pigmentosum which predisposes to skin cancer. Mice with defective DNA repair were generated by targeting the excision

repair cross complementing gene (ERCC-1) in the embryonic stem cell line, HM-1. Homozygous ERCC-1 mutants were runted at birth and died before weaning with liver failure. Examination of organs revealed polyploidy in perinatal liver, progressing to severe aneuploidy by 3 weeks of age. Elevated p53 levels were detected in liver, brain and kidney, supporting the hypothesised role for %%%p53%%% as a monitor of %%%DNA%%% %%%damage%%%.

14/3,AB/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09202105 BIOSIS NO.: 199497210475
UV-induced nuclear accumulation of the %%%p53%%% protein is evoked through
%%%DNA%%% %%%damage%%% of actively transcribed genes.

AUTHOR: Yamaizumi Masaru; Sugano Tatsuo
AUTHOR ADDRESS: Inst. Mol. Embryol. Genet., Kumamoto Univ. Sch. Med.,
Kumamoto 862, Japan

JOURNAL: Journal of Radiation Research 34 (4):p323 1993

CONFERENCE/MEETING: 36th Annual Meeting of the Japan Radiation Research
Society Hiroshima, Japan October 27-29, 1993
ISSN: 0449-3060
RECORD TYPE: Citation
LANGUAGE: English

14/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09068605 BIOSIS NO.: 199497076975
Point mutations of the P53 gene, human hepatocellular carcinoma and aflatoxins.

AUTHOR: Gerbes Alexander L(a); Caselmann Wolfgang H
AUTHOR ADDRESS: (a)Dep. Med. II, Klinikum Grosshadern, Univ. Munich,
Marchioninistr. 15, 81366 Munich, Germany

JOURNAL: Journal of Hepatology 19 (2):p312-315 1993
ISSN: 0168-8278
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The tumor suppressor %%%p53%%% exerts important protective
functions towards %%%DNA%%%-%%%damaging%%% agents. Its inactivation by
allelic deletions or point mutations within the P53 gene as well as complex formation of wildtype p53 with cellular or viral proteins is a common and crucial event in carcinogenesis. Mutations increase the half-life of the p53 protein allowing the immunohistochemical detection and anti-p53 antibody formation. Distinct G to T point mutations in codon 249 leading to a substitution of the basic amino acid arginine by the neutral amino acid serin are responsible for the altered functionality of the mutant gene product and were originally identified in 8 of 16 Chinese and 5 of 10 African HCC patients. Both groups are frequently exposed to mycotoxin contaminations of their food. Today an average P53 gene mutation rate of 25% is assumed for high-aflatoxin B-1-exposure regions. This is double the rate observed in low-aflatoxin B-1-exposure countries. Although many HCC patients displaying P53 mutations also suffer from HBV infection, which itself can lead to rearrangements of P53 coding regions or induce the synthesis of viral proteins possibly interacting with p53, the specific G to T transversion within codon 249 of the P53 gene seems to directly reflect the extent of aflatoxin B-1 exposure.

14/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09065911 BIOSIS NO.: 199497074281
Differential induction of transcriptionally active p53 following UV or ionizing radiation: Defects in chromosome instability syndromes?

AUTHOR: Lu Xin; Lane David P
AUTHOR ADDRESS: Cell Transformation Res. Group, Cancer Res. Campaign Lab.,
Dep. Biochem., Univ. Dundee, Dundee DD1 4, UK

JOURNAL: Cell 75 (4):p765-778 1993
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Accumulation of %%%p53%%% protein was seen in the nuclei of
mammalian cells following %%%DNA%%% %%%damage%%% caused by ultraviolet
radiation (UV), X-ray, or a restriction enzyme. Promoters containing %%%p53%%%-binding sites show a dramatic transcriptional response to %%%DNA%%% %%%damage%%%. The p53 response to X-ray is rapid, reaching a
peak at 2 hr after radiation, but is very transitory and reduced in magnitude compared with that seen in response to UV. We find no substantive defect in the p53 response of cells from ataxia telangiectasia or xeroderma pigmentosum complementation group A patients. In contrast, 2 out of 11 primary cultures from Bloom's patients showed a complete absence of p53 accumulation following UV irradiation or SV40 infection and a grossly delayed and aberrant response following X-ray.

14/3,AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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09021729 BIOSIS NO.: 199497030099
Increased sequence-specific %%%p53%%%-DNA binding activity after %%%DNA%%%
%%%damage%%% is attenuated by phorbol esters.

AUTHOR: Price Brendan D(a); Calderwood Stuart K
AUTHOR ADDRESS: (a)Stress Protein Group, Dana-Farber Cancer Inst., 44 Binney St., Boston, MA 02115, USA

JOURNAL: Oncogene 8 (11):p3055-3062 1993
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Damage to cellular DNA greatly increases the levels of the tumor-suppressor gene p53 and induces cell cycle arrest in G-1. A critical function of wild-type p53 is its ability to bind to specific DNA sequences. The effect of DNA damage on the sequence-specific DNA-binding properties of cellular p53 was investigated using DNA gel mobility-shift assays with nuclear extracts from NIH3T3 cells. DNA damage (initiated by radiation) induced a rapid, cycloheximide-sensitive increase in the levels of nuclear p53-DNA binding activity and an increase in the half-life of the p53 protein. Increased p53-DNA binding activity could be detected at low (0.2 Gy), non-lethal doses of radiation. The tumor promoter 12-O-tetradecanoyl phorbol 13-acetate (TPA) attenuated the DNA damage-induced increase in p53-DNA binding activity by decreasing the half-life of the p53 protein. The tumor promoter properties of TPA may therefore be mediated by interfering with the cellular %%%p53%%% response
to %%%DNA%%% %%%damage%%%. The increased levels of %%%p53%%% bound to
specific DNA sequences following %%%DNA%%% %%%damage%%% may induce cell
cycle arrest. p53-mediated growth arrest could occur by inhibition of DNA replication and/or alterations in transcription of cell cycle genes.

14/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08962963 BIOSIS NO.: 199396114464

Loss of a %%%p53%%%-associated G1 checkpoint does not decrease cell survival following %%%DNA%%% %%%damage%%%.

AUTHOR: Slichenmyer William J; Nelson William G; Slebos Robert J; Kastan
Michael B(a)
AUTHOR ADDRESS: (a)Dep. Oncol., Johns Hopkins Univ. Sch. Med., Baltimore,
MD 21287, USA

JOURNAL: Cancer Research 53 (18):p4164-4168 1993
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cell cycle checkpoints regulate progression through the cell cycle. In yeast, loss of the G-2 checkpoint by mutation of the rad9 gene results in increased genetic instability as well as increased sensitivity to ionizing radiation. In contrast, comparing clonogenic survival of cells which are isogeneic except for p53 functional status, we find that loss of a G-1 checkpoint in mammalian cells is not associated with increased sensitivity to the lethal effects of ionizing radiation or a topoisomerase I inhibitor, camptothecin. These results indicate that increased sensitivity to DNA-damaging agents is not necessarily a defining feature of a mammalian cell cycle checkpoint. Furthermore, in light of a recent link of p53 function to radiation-induced apoptosis in hematopoietic cells, these observations suggest that p53-dependent apoptosis is a cell type-specific phenomenon and thus predict that the biological consequences of loss of p53 function will be cell type specific.

14/3,AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08901955 BIOSIS NO.: 199396053456
P53 mutations increase resistance to ionizing radiation.

AUTHOR: Lee Jonathan M; Bernstein Alan(a)
AUTHOR ADDRESS: (a)Div. Molecular Developmental Biol., Samuel Lunenfeld
Res. Inst., Mount Sinai Hosp., 600 Universi

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 90 (12):p5742-5746 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mouse and human tumors of diverse origin frequently have somatically acquired mutations or rearrangements of the p53 gene, or they have lost one or both copies of the gene. Although wild-type p53 protein is believed to function as a tumor-suppressor gene, it is as yet unclear how p53 mutations lead to neoplastic development. Wild-type p53 has been postulated to play a role in DNA repair, suggesting that expression of mutant forms of %%%p53%%% might alter cellular resistance to the %%%DNA%%% %%%damage%%% caused by gamma radiation. Moreover, p53 is
thought to function as a cell cycle checkpoint after irradiation, also suggesting that mutant p53 might change the cellular proliferative response to radiation. We have used transgenic mice expressing one of two mutant alleles of p53 to test this prediction. Our results show that expression of both mutant variants of the mouse p53 gene significantly increases the cellular resistance of a variety of hematopoietic cell lineages to gamma radiation. These observations provide direct evidence that %%%p53%%% mutations affect the cellular response to %%%DNA%%%
%%%damage%%%, either by increasing DNA repair processes or, possibly, by
increasing cellular tolerance to DNA damage. The association of p53 mutations with increased radioresistance suggests possible mechanisms through which alterations in the p53 gene might lead to oncogenic transformation.

14/3,AB/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08899903 BIOSIS NO.: 199396051404
Induction of cellular %%%p53%%% activity by %%%DNA%%%-%%%damaging%%% agents
and growth arrest.

AUTHOR: Zhan Qimin; Carrier France; Fornace Albert J Jr(a)
AUTHOR ADDRESS: (a)Lab. Mol. Pharmacol., DTP, DCT, Natl. Cancer Inst., Room
5C09, Build. 37, Bethesda, MD 20892, USA

JOURNAL: Molecular and Cellular Biology 13 (7):p4242-4250 1993
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The tumor suppressor p53 can function as a sequence-specific transcription factor and is required for activation by ionizing radiation (IR) of one or more downstream effector genes, such as the human GADD45 gene. One important consequence of IR that is probably mediated by these downstream effector genes is activation of the p53-mediated G-1 cell cycle checkpoint. While the induction of reporter constructs containing p53-binding sites has already been demonstrated with p53 expression vectors, we have now demonstrated the direct activation of such a construct after treatment of the human RKO line, which has a normal %%%p53%%% phenotype, with various types of %%%DNA%%%-%%%damaging%%%
agents and also after growth arrest produced by medium depletion (starvation). IR, UV radiation, and methylmethane sulfonate were found to induce p53 activity when a stably integrated reporter construct containing functional p53-binding sites was used and also in mobility shift assays with a p53-binding site from the GADD45 gene, and IR-inducible gene previously associated with growth arrest. The same cell treatments that induced this p53 activity also caused an increase in cellular p53 protein levels. The response in cells lacking normal p53 or in RKO cells expressing a dominant negative mutant p53 was markedly reduced. Interestingly, the spectrum of effective inducing agents for the above-described experiments was similar to that which induces GADD45 either in cells with a normal p53 status or, with the exception of IR, in cells lacking normal p53. These results indicate a role for pS3 in the IR pathway, which is completely p53 dependent, and in other genotoxic stress responses, in which p53 has a cooperative effect but is not required.

14/3,AB/9 (Item 9 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08879266 BIOSIS NO.: 199396030767
Increases in sequence specific DNA binding by %%%p53%%% following treatment
with chemotherapeutic and %%%DNA%%% %%%damaging%%% agents.

AUTHOR: Tishler Roy B(a); Calderwood Stuart K; Coleman C Norman; Price Brendan D
AUTHOR ADDRESS: (a)Joint Center Radiation Therapy, 50 Binney St., Boston,
MA 02115, USA

JOURNAL: Cancer Research 53 (10):p2212-2216 1993
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have investigated the effect of chemotherapeutic and DNA damaging agents on binding of the tumor suppressor phosphoprotein p53 to its consensus DNA sequence. Activation of p53-DNA binding was seen for treatment with radiation, hydrogen peroxide, actinomycin D, Adriamycin, etoposide, camptothecin, 5-fluorouracil, mitomycin C, and cisplatin. These results showed that DNA strand breaks were sufficient to lead to increased levels of p53. The protein synthesis inhibitor cycloheximide blocks the increase in %%%p53%%% following %%%DNA%%% %%%damage%%%. The
increase in p53 activation in camptothecin treated cells may result, at least in part, from an increased half-life of the protein and consequent

increases in intracellular protein concentration.

14/3,AB/10 (Item 10 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08878801 BIOSIS NO.: 199396030302
Human papillomavirus 16 E6 expression disrupts the %%%p53%%%-mediated
cellular response to %%%DNA%%% %%%damage%%%.

AUTHOR: Kessis Theodore D; Slebos Robbert J; Nelson William G; Kastan Michael B; Plunkett Beverly S; Han Sung M; Lorincz Attila T; Hedrick Lora (a); Cho Kathleen R(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Johns Hopkins Univ. Sch. Med., Baltimore,
MD 21205, USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 90 (9):p3988-3992 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Infection with certain types of human papillomaviruses (HPV) is highly associated with carcinomas of the human uterine cervix. However, HPV infection alone does not appear to be sufficient for the process of malignant transformation, suggesting the requirement of additional cellular events. After DNA damage, normal mammalian cells exhibit G-1 cell-cycle arrest and inhibition of replicative DNA synthesis. This mechanism, which requires wild-type p53, presumably allows cells to undertake DNA repair and avoid the fixation of mutations. We directly tested whether the normal response of cervical epithelial cells to DNA damage may be undermined by interactions between the E6 protein expressed by oncogenic HPV types and wild-type %%%p53%%%. We treated primary keratinocytes with the %%%DNA%%%-%%%damaging%%% agent actinomycin D and
demonstrated inhibition of replicative DNA synthesis and a significant increase in p53 protein levels. In contrast, inhibition of DNA synthesis and increases in p53 protein did not occur after actinomycin D treatment of keratinocytes immortalized with HPV16 E6/E7 or in cervical carcinoma cell lines containing HPV16, HPV18, or mutant p53 alone. To test the effects of E6 alone on the cellular response to DNA damage, HPV16 E6 was expressed in the carcinoma cell line RKO, resulting in undetectable baseline levels of p53 protein and loss of the G, arrest that normally occurs in these cells after DNA damage. These findings demonstrate that oncogenic E6 can disrupt an important cellular response to DNA damage mediated by p53 and may contribute to the subsequent accumulation of genetic changes associated with cervical tumorigenesis.

14/3,AB/11 (Item 11 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08821082 BIOSIS NO.: 199395110433
Distinct pattern of p53 mutations in bladder cancer: Relationship to tobacco usage.

AUTHOR: Spruck Charles H III; Rideout William M III; Olumi Aria F; Ohneseit
Petra F; Yang Allen S; Tsai Yvonne C; Nichols Peter W; Horn Thomas; Hermann Gregers G; et al
AUTHOR ADDRESS: Inq.: Kenneth Norris, Jr., Comprehensive Cancer Cent.,
Univ. Southern Calif., 1441 Eastlake Avenue, ,

JOURNAL: Cancer Research 53 (5):p1162-1166 1993
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A distinct mutational spectrum for the p53 tumor suppressor gene
in bladder carcinomas was established in patients with known exposures to cigarette smoke. Single-strand conformational polymorphism analysis of exons 5 through 8 of the p53 gene showed inactivating mutations in 16 of 40 (40%) bladder tumors from smokers and 13 of 40 (33%) tumors from lifetime nonsmokers. Overall, 13 of the 50 (26%) total point mutations discovered in this and previous work were G:C fwdarw C:G transversions, a relatively rare mutational type in human tumors. In six tumors, identical AGA (Arg) fwdarw ACA (Thr) point mutations at codon 280 were observed, suggesting a mutational hotspot in these tumors. Comparison of the mutational spectra from smokers and nonsmokers revealed no obvious differences in the types or positions of inactivating mutations; however, 5 of 15 tumors containing point mutations from cigarette smokers had double mutations, four of which were tandem mutations on the same allele. No double mutations were found in tumors from nonsmoking patients. None of the mutations in smokers were G:C fwdarw T:A transversions, which would be anticipated for exposure to the suspected cigarette smoke carcinogen 4-aminobiphenyl. The result suggest that, although cigarette smoke exposure may not significantly alter the kinds of mutations sustained in the %%%p53%%% gene, it may act to increase the extent of %%%DNA%%% %%%damage%%% per mutagenic event.

14/3,AB/12 (Item 12 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08798458 BIOSIS NO.: 199395087809
Induction of nuclear accumulation of the tumor-suppressor protein %%%p53%%%
by %%%DNA%%%-%%%damaging%%% agents.

AUTHOR: Fritsche Michael; Haessler Christel; Brandner Gerhard(a)
AUTHOR ADDRESS: (a)Abteilung Virologie, Inst. fuer Medizinische Mikrobiologie und Hygiene der Universitaet, P.O.B. , Germany

JOURNAL: Oncogene 8 (2):p307-318 1993
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

RC268.42 B48 A Innis

ABSTRACT: Cancer therapy drugs, such as diamminedichloroplatinum (cisplatin), mitomycin C, etoposide and a number of other compounds, as well as energy-rich radiation, are known to act on cellular DNA. These agents are shown to induce nuclear accumulation of the so-called tumor-suppressor protein p53 in fibroblastoid cells, as well as in epithelioid normal and immortalized cells of murine, simian, and human origin. p53 accumulation starts a few hours after treatment and can remain detectable in surviving cells for at least 20 days. Accumulation occurs because of increased p53 protein stability and depends on ongoing translation. It is not the result of enhanced gene expression. A number of cell cycle inhibitors do not affect p53 protein accumulation, suggesting that the process may start from several points in the cell cycle. Since the increase in the nuclear p53 protein levels occurs within a few hours in most of the treated normal diploid cells, it is unlikely that the accumulated p53 protein is derived from a mutated p53 gene. The results obtained are in accordance with the view that the DNA damage-induced p53 accumulation may either inhibit cell growth, allowing DNA repair process, or, in the case of severe damage, initiate apopotosis.

14/3,AB/13 (Item 13 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08798026 BIOSIS NO.: 199395087377
High levels of p53 protein in UV-irradiated normal human skin.

AUTHOR: Hall Peter A(a); McKee Philip H; Menage Helene D; Dover Robin; Lane
David P
AUTHOR ADDRESS: (a)Dep. Histopathology, UMDS, St. Thomas's Campus, Lambeth
Palace Road, London SE1 7EH, UK

JOURNAL: Oncogene 8 (1):p203-207 1993
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Exposure of normal adult human skin to doses of UV irradiation that induced mild sunburn resulted in the rapid appearance of p53 protein in the epidermis and superficial dermal fibroblasts. Immunohistological analysis with a panel of antibodies established that while p53 staining was not seen in normal skin it appeared within 2 h of UV exposure. The level of p53 immunostaining peaked at 24 h and returned to undetectable levels within 360 h. The induction of proliferating cell nuclear antigen (PCNA)(which is required for both DNA replication and repair) followed a similar spatial and temporal pattern to p53. The UV irradiation did not induce a mitotic response or the replication-associated antigens DNA polymerase alpha or Ki67. The accumulation of high levels of p53 and PCNA in response to UV doses to which many human populations are routinely exposed provides strong support for a model in which normal %%%p53%%% acts as part of the %%%DNA%%% %%%damage%%% response in vertebrate cells.

Such a model is consistent with the profound tumor-suppressor function of the p53 gene, the high rate of p53 mutation in neoplasia and the exceptionally high tumor susceptibility of p53-deficient mice.

14/3,AB/14 (Item 14 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08641860 BIOSIS NO.: 199345059935
Human papilloma virus 16 E6 oncoprotein decreases %%%p53%%% protein levels
and blocks the %%%p53%%% mediated response to %%%DNA%%% %%%damage%%% in
RKO cells.

AUTHOR: Slebos R; Kessis T; Plunkett B; Han S; Kastan M; Hedrick L; Cho K
AUTHOR ADDRESS: The Johns Hopkins Univ., Dep. Pathol., Baltimore, MD 21287
, USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual
Meeting 34 (0):p544 1993

CONFERENCE/MEETING: 84th Annual Meeting of the American Association for
Cancer Research Orlando, Florida, USA May 19-22, 1993
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

14/3,AB/15 (Item 15 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1999 BIOSIS. All rts. reserv.

08601213 BIOSIS NO.: 199345019288
%%%P53%%%-Deficient embryonic fibroblasts exhibit decreased sensitivity to
%%%DNA%%% %%%damage%%% and altered cell cycle control.

AUTHOR: Sands Arthur T; Donehower Lawrence A; Bradley Allan
AUTHOR ADDRESS: Dep. Molecular Genetics, Baylor Coll. Med., Houston, TX
77030, USA

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (17 PART E):p246
1993

QH506.J67
Film

CONFERENCE/MEETING: Keystone Symposium on Gene Therapy Keystone, Colorado,
USA April 12-18, 1993
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English

14/3,AB/16 (Item 16 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1999 BIOSIS. All rts. reserv.

08563155 BIOSIS NO.: 199344113155
Identification of a %%%p53%%%-regulated gene involved in a cell-cycle checkpoint activated by %%%DNA%%% %%%damage%%%.

AUTHOR: Zhan Qimin; Kastan Michael B; Carrier France; Hollander M Christine
; Fornace Albert J Jr
AUTHOR ADDRESS: Lab. Mol. Pharmacol., NIH, Bethesda, MD, USA

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (17 PART A):p141
1993

CONFERENCE/MEETING: Keystone Symposium on Transcription: Factors, Regulation and Differentiation Keystone, Colorado, USA January 17-24, 1993
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English

14/3,AB/17 (Item 17 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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08563135 BIOSIS NO.: 199344113135
Characterization of the Drosophila homologue of the %%%p53%%% anti-oncogene
and its response to %%%DNA%%% %%%damage%%%.

AUTHOR: Dusenbery Ruth L; Yakes F Michael
AUTHOR ADDRESS: Dep. Chem., Wayne State Univ., Detroit, MI 48202, USA

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (17 PART A):p136
1993

CONFERENCE/MEETING: Keystone Symposium on Transcription: Factors, Regulation and Differentiation Keystone, Colorado, USA January 17-24, 1993
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English

14/3,AB/18 (Item 18 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1999 BIOSIS. All rts. reserv.

08265234 BIOSIS NO.: 000043042507
%%%P53%%% PROTEIN IS A CELL CYCLE CHECKPOINT FOLLOWING %%%DNA%%%
%%%DAMAGE%%%

AUTHOR: KASTAN M B; PLUNKETT B S; KUERBITZ S J
AUTHOR ADDRESS: JOHNS HOPKINS ONCOL. CENT., BALTIMORE, MD. 21205.

JOURNAL: 83RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER
RESEARCH, SAN DIEGO, CALIFORNIA, USA, MAY 20-23, 1992. PROC AM ASSOC CANCER
RES ANNU MEET 33 (0). 1992. 169.
CODEN: PAMRE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

14/3,AB/19 (Item 19 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07974897 BIOSIS NO.: 000093042475
PARTICIPATION OF %%%P53%%% PROTEIN IN THE CELLULAR RESPONSE TO %%%DNA%%%
%%%DAMAGE%%%

AUTHOR: KASTAN M B; ONYEKWERE O; SIDRANSKY D; VOGELSTEIN B; CRAIG R W
AUTHOR ADDRESS: ONCOL. 3-120, JOHNS HOPKINS HOSP., 600 NORTH WOLFE ST.,
BALTIMORE, MD. 21205.

JOURNAL: CANCER RES 51 (23 PART 1). 1991. 6304-6311.
FULL JOURNAL NAME: Cancer Research
CODEN: CNREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The inhibition of replicative DNA synthesis that follows DNA damage may be critical for avoiding genetic lesions that could contribute to cellular transformation. Exposure of ML-1 myeloblastic leukemia cells to nonlethal doses of the DNA damaging agents, .gamma.-irradiation or actinomycin D, causes a transient inhibition of replicative DNA synthesis via both G1 and G2 arrests. Levels of p53 protein in ML-1 cells and in proliferating normal bone marrow myeloid progenitor cells increase and decrease in temporal association with the G1 arrest. In contrast, the S-phase arrest of ML-1 cells caused by exposure to the anti-metabolite, cytosine arabinoside, which does not directly damage DNA, is not associated with a significant change in p53 protein levels. Caffeine treatment blocks both the G1 arrest and the induction of p53 protein after .gamma.-irradiation, thus suggesting that blocking the induction of p53 protein may contribute to the previously observed effects of caffeine on cell cycle changes after DNA damage. Unlike ML-1 cells and normal bone marrow myeloid progenitor cells, hematopoietic cells that either lack p53 gene expression or overexpress a mutant form of the p53 gene do not exhibit a G1 arrest after .gamma.-irradiation; however, the G2 arrest is unaffected by the status of the p53 gene. These results suggest a role for the wild-type %%%p53%%% protein in the inhibition of DNA synthesis that follows %%%DNA%%% %%%damage%%% and thus suggest a new mechanism for
how the loss of wild-type p53 might contribute to tumorigenesis.

14/3,AB/20 (Item 20 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07737442 BIOSIS NO.: 000041046238
FROM GENE TO CARCINOGEN A RAPIDLY EVOLVING FIELD IN MOLECULAR EPIDEMIOLOGY

AUTHOR: JONES P A; BUCKLEY J D; HENDERSON B E; ROSS R K; PIKE M C
AUTHOR ADDRESS: INST. ANIM. PHYSIOL. GENETICS RES., BABRAHAM, CAMBRIDGE CB2
4AT, UK.

JOURNAL: CANCER RES 51 (13). 1991. 3617-3620.
FULL JOURNAL NAME: Cancer Research
CODEN: CNREA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

14/3,AB/21 (Item 21 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07510622 BIOSIS NO.: 000040067556
ONCOGENES IN HUMAN LUNG CANCER

AUTHOR: KAYE F J; BARKSDALE S K; HARBOUR J W; MINNA J D
AUTHOR ADDRESS: NCI-NAVY MED. ONCOL. BRANCH, NATL. CANCER INST. AND NAVAL
HOSP., BETHESDA, MD. 20814, USA.

JOURNAL: SLUYSER, M. (ED.). ELLIS HORWOOD SERIES IN MOLECULAR BIOLOGY:
MOLECULAR BIOLOGY OF CANCER GENES. 292P. ELLIS HORWOOD LTD.: CHICHESTER,
ENGLAND, UK; NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-13-599614-7. 0 (0).
1990. 207-222.
CODEN: 31955
RECORD TYPE: Citation
LANGUAGE: ENGLISH

14/3,AB/22 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1999 Elsevier Science B.V. All rts. reserv.

05667527 EMBASE No: 1994066662
%%%p53%%%: A determinant of the cell cycle response to %%%DNA%%%
%%%damage%%%
Kastan M.B.
Johns Hopkins Oncology Center,Baltimore, MD 21287 United States
Advances in Experimental Medicine and Biology (ADV. EXP. MED. BIOL.) (
United States) 1993, 339/- (291-293)

CODEN: AEMBA ISSN: 0065-2598
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH

14/3,AB/23 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1999 Elsevier Science B.V. All rts. reserv.

05492607 EMBASE No: 1993260706
Erratum: Induction of cellular %%%p53%%% activity by %%%DNA%%%-%%%damaging%%% agents and growth arrest (Molecular and Cellular Biology
13:7 (4249))
Zhan Q.; Carrier F.; Fornace Jr. A.J.
Laboratory of Molecular Pharmacology, DTP, National Cancer Institute,Bethesda, MD 20892 United States
Molecular and Cellular Biology (MOL. CELL. BIOL.) (United States) 1993, 13/9 (5928)

CODEN: MCEBD ISSN: 0270-7306
DOCUMENT TYPE: Journal; Erratum
LANGUAGE: ENGLISH

14/3,AB/24 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1999 Elsevier Science B.V. All rts. reserv.

05484307 EMBASE No: 1993252406
Erratum: Induction of nuclear accumulation of the tumor-suppressor protein %%%p53%%% by %%%DNA%%%-%%%damaging%%% agents (Oncogene (1993) 8
(307-318))
Fritsche; et al.
Oncogene (ONCOGENE) (United Kingdom) 1993, 8/9 (2605)

CODEN: ONCNE ISSN: 0950-9232
DOCUMENT TYPE: Journal; Erratum
LANGUAGE: ENGLISH

14/3,AB/25 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
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05319838 EMBASE No: 1993087923
Distinct pattern of p53 mutations in bladder cancer: Relationship to tobacco usage
Spruck III C.H.; Rideout III W.M.; Olumi A.F.; Ohneseit P.F.; Yang A.S.; Tsai Y.C.; Nichols P.W.; Horn T.; Hermann G.G.; Steven K.; Ross R.K.; Yu M.C.; Jones P.A.
K. Norris Jr. Comprehen. Cancer Ctr., University of Southern California, 1441 Eastlake Avenue,Los Angeles, CA 90033-0800 United States
Cancer Research (CANCER RES.) (United States) 1993, 53/5 (1162-1166)

CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A distinct mutational spectrum for the p53 tumor suppressor gene in bladder carcinomas was established in patients with known exposures to

cigarette smoke. Single-strand conformational polymorphism analysis of exons 5 through 8 of the p53 gene showed inactivating mutations in 16 of 40 (40%) bladder tumors from smokers and 13 of 40 (33%) tumors from lifetime nonsmokers. Overall, 13 of the 50 (26%) total point mutations discovered in this and previous work were G:C <rt arrow> C:G transversions, a relatively rare mutational type in human tumors. In six tumors, identical AGA (Arg) <rt arrow> ACA (Thr) point mutations at codon 280 were observed, suggesting a mutational hotspot in these tumors. Comparison of the mutational spectra from smokers and nonsmokers revealed no obvious differences in the types or positions of inactivating mutations; however, 5 of 15 tumors containing point mutations from cigarette smokers had double mutations, four of which were tandem mutations on the same allele. No double mutations were found in tumors from nonsmoking patients. None of the mutations in smokers were G:C <rt arrow> T:A transversions, which would be anticipated for exposure to the suspected cigarette smoke carcinogen 4-aminobiphenyl. The results suggest that, although cigarette smoke exposure may not significantly alter the kinds of mutations sustained in the %%%p53%%% gene, it may act to increase the extent of %%%DNA%%% %%%damage%%% per mutagenic event.

14/3,AB/26 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

07714212 94100973
Mice with DNA repair gene (ERCC-1) deficiency have elevated levels of p53, liver nuclear abnormalities and die before weaning [see comments]
McWhir J; Selfridge J; Harrison DJ; Squires S; Melton DW
Institute of Cell and Molecular Biology, University of Edinburgh, UK.
Nat Genet (UNITED STATES) Nov %%%1993%%%, 5 (3) p217-24, ISSN
1061-4036 Journal Code: BRO
Comment in Nat Genet 1993 Nov;5(3):207-8
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Defects in nucleotide excision repair are associated with the human condition xeroderma pigmentosum which predisposes to skin cancer. Mice with defective DNA repair were generated by targeting the excision repair cross complementing gene (ERCC-1) in the embryonic stem cell line, HM-1. Homozygous ERCC-1 mutants were runted at birth and died before weaning with
liver failure. Examination of organs revealed polyploidy in perinatal liver, progressing to severe aneuploidy by 3 weeks of age. Elevated p53 levels were detected in liver, brain and kidney, supporting the hypothesised role for %%%p53%%% as a monitor of %%%DNA%%% %%%damage%%%.

14/3,AB/27 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

07550494 93262076
Tumour suppressor genes and molecular chaperones.
Lane DP; Midgley C; Hupp T
Department of Biochemistry, University of Dundee, U.K.
Philos Trans R Soc Lond B Biol Sci (ENGLAND) Mar 29 %%%1993%%%, 339
(1289) p369-72; discussion 372-3, ISSN 0962-8436 Journal Code: P5Z
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The two tumour suppressor genes that are most commonly inactivated in human cancer are the p53 gene on chromosome 17 and the retinoblastoma (Rb) gene on chromosome 11. Recent studies of both gene products suggest that they are able to act as powerful negative regulators of cell division. The Rb gene seems to exert this activity by physically complexing to a variety of specific transcription factors and inactivating their function. The capacity of Rb protein to bind these factors is regulated by phosphorylation. The Rb protein can therefore be seen to act as a chaperone for these factors. The p53 protein also may act in part by regulating transcription but may also interact directly with the DNA replication apparatus. The growth suppressive function of %%%p53%%% is induced by
%%%DNA%%% %%%damage%%% leading to an attractive model of p53 as an
essential checkpoint control. The p53 protein interacts with members of the hsp70 chaperone family which we now show can regulate its function.

14/3,AB/28 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

07504290 93177698
Distinct pattern of p53 mutations in bladder cancer: relationship to tobacco usage [published erratum appears in Cancer Res 1993 May 15;53(10 Suppl):2427]
Spruck CH 3d; Rideout WM 3d; Olumi AF; Ohneseit PF; Yang AS; Tsai YC;
Nichols PW; Horn T; Hermann GG; Steven K; et al
Kenneth Norris Jr. Comprehensive Cancer Center, Urologic Cancer Research Laboratory, University of Southern California, Los Angeles 90033.
Cancer Res (UNITED STATES) Mar 1 %%%1993%%%, 53 (5) p1162-6, ISSN
0008-5472 Journal Code: CNF
Contract/Grant No.: R01 CA40468, CA, NCI; R35 CA49758, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A distinct mutational spectrum for the p53 tumor suppressor gene in bladder carcinomas was established in patients with known exposures to cigarette smoke. Single-strand conformational polymorphism analysis of exons 5 through 8 of the p53 gene showed inactivating mutations in 16 of 40 (40%) bladder tumors from smokers and 13 of 40 (33%) tumors from lifetime nonsmokers. Overall, 13 of the 50 (26%) total point mutations discovered in this and previous work were G:C-->C:G transversions, a relatively rare mutational type in human tumors. In six tumors, identical AGA (Arg)-->ACA (Thr) point mutations at codon 280 were observed, suggesting a mutational hotspot in these tumors. Comparison of the mutational spectra from smokers and nonsmokers revealed no obvious differences in the types or positions of inactivating mutations; however, 5 of 15 tumors containing point mutations from cigarette smokers had double mutations, four of which were tandem mutations on the same allele. No double mutations were found in tumors from nonsmoking patients. None of the mutations in smokers were G:C-->T:A transversions, which would be anticipated for exposure to the suspected cigarette smoke carcinogen 4-aminobiphenyl. The results suggest that, although cigarette smoke exposure may not significantly alter the kinds of mutations sustained in the %%%p53%%% gene, it may act to increase the extent of %%%DNA%%% %%%damage%%% per mutagenic event.

14/3,AB/29 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

121006182 CA: 121(1)6182z JOURNAL
Control of G1 arrest after DNA damage
AUTHOR(S): Kastan, Michael B.; Kuerbitz, Steven J.
LOCATION: Johns Hopkins Oncol. Cent., Johns Hopkins Hosp., Baltimore, MD,
21205, USA
JOURNAL: Environ. Health Perspect. DATE: 1993 VOLUME: 101 NUMBER: 5
PAGES: 55-8 CODEN: EVHPAZ ISSN: 0091-6765 LANGUAGE: English

14/3,AB/30 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

120184326 CA: 120(15)184326m JOURNAL
Cloning and characterization of chromosomal copy of the gene encoding a murine homolog of human GADD45, a protein induced by DNA damage
AUTHOR(S): Alimzhanov, M. B.; Kuprash, D. V.; Turetskaya, R. L.; Osipovich, O. A.; Borodulina, O. R.; Osovskaya, V. S.; Chumakov, P. M.; Nedospasov, S. A.
LOCATION: Inst. Mol. Biol., Moscow, Russia,
JOURNAL: Dokl. Akad. Nauk DATE: 1993 VOLUME: 333 NUMBER: 6 PAGES:
788-91 CODEN: DAKNEQ LANGUAGE: Russian

14/3,AB/31 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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120100688 CA: 120(9)100688v JOURNAL
Induction of cellular p53 activity by DNA-damaging agents and growth arrest. (Erratum to document cited in CA119(19):198646g)

AUTHOR(S): Zhan, Qimin; Carrier, France; Fornace, Albert, J., Jr.
LOCATION: Lab. Mol. Pharmacol., Natl. Cancer Inst., Bethesda, MD, 20892,
USA
JOURNAL: Mol. Cell. Biol. DATE: 1993 VOLUME: 13 NUMBER: 9 PAGES: 5928
CODEN: MCEBD4 ISSN: 0270-7306 LANGUAGE: English

14/3,AB/32 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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119241051 CA: 119(23)241051y JOURNAL
Induction of nuclear accumulation of the tumor-suppressor protein p53 by DNA-damaging agents. (Erratum to document cited in CA118(15):139404h)
AUTHOR(S): Fritsche, Michael; Haessler, Christel; Brandner, Gerhard
LOCATION: Inst. Med. Mikrobiol. Hyg., Univ. Freiburg, Freiburg, Germany,
JOURNAL: Oncogene DATE: 1993 VOLUME: 8 NUMBER: 9 PAGES: 2605 CODEN:
ONCNES ISSN: 0950-9232 LANGUAGE: English

14/3,AB/33 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

119218373 CA: 119(21)218373w JOURNAL
Mechanisms of action of p53
AUTHOR(S): Barak, Y.; Ginsberg, D.; Michael, D.; Ragimov, N.; Shaulian, E.; Yonish-Rouach, E.; Zauberman, A.; Aloni, Y.; Oren, M.
LOCATION: Dep. Chem. Immunol., Weizmann Inst. Sci., 76100, Rehovot, Israel
JOURNAL: Int. Congr. Ser. - Excerpta Med. DATE: 1993 VOLUME: 1016
NUMBER: Pharmacology of Cell Differentiation PAGES: 129-45 CODEN: EXMDA4 ISSN: 0531-5131 LANGUAGE: English

14/3,AB/34 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1999 American Chemical Society. All rts. reserv.

118117563 CA: 118(13)117563g JOURNAL
Worrying about p53
AUTHOR(S): Lane, David P.
LOCATION: Cancer Res. Lab., Univ. Dundee, Dundee, UK, DD1 4HN
JOURNAL: Curr. Biol. DATE: 1992 VOLUME: 2 NUMBER: 11 PAGES: 581-3
CODEN: CUBLE2 ISSN: 0960-9822 LANGUAGE: English
? log

08/918407
A449

Set Items Description
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? s p53

S1 50803 P53
? s adenovir?

S2 57182 ADENOVIR?
? s s1(5n)s2

50803 S1
57182 S2
S3 766 S1(5N)S2
? s s3 and py<=1990

Processing
Processing
Processing
766 S3
33689832 PY<=1990
S4 36 S3 AND PY<=1990
? rd

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S5 16 RD (unique items)
? t s5/3,ab/1-16

5/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07423210 BIOSIS NO.: 000091029199
DOMAINS REQUIRED FOR IN-VITRO ASSOCIATION BETWEEN THE CELLULAR %%%P53%%%
AND THE %%%ADENOVIRUS%%% 2 E1B 55K PROTEINS

AUTHOR: KAO C C; YEW P R; BERK A J
AUTHOR ADDRESS: DEP. OF MICROBIOL. MOL. GENETICS, MOL. BIOL. INST., UNIV.
OF CALIFORNIA, LOS ANGELES, CALIF. 90024-1570.

JOURNAL: VIROLOGY 179 (2). 1990. 806-814.
FULL JOURNAL NAME: Virology
CODEN: VIRLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The 55K protein encoded by the adenovirus 2 E1B gene is required
for complete cellular transformation and binds the cellular protein p53. Using an in vitro immunoprecipitation assay, we mapped the domains in both 55K and p53 required for the interaction of the two proteins. The domain in p53 mapped to the amino terminal 123 residues. There are several domains in the 495 residue polypeptide which contribute to stable association with p53, with the most essential region mapping between residues 224 and 354. Mutations which prevented 55K-p53 binding were not more defective for transformation than other mutations which did not affect binding.

5/3,AB/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07302263 BIOSIS NO.: 000090082150
TRANSACTIVATION OF THE P53 ONCOGENE BY E1A GENE PRODUCTS

AUTHOR: BRAITHWAITE A; NELSON C; SKULIMOWSKI A; MCGOVERN J; PIGOTT D;
JENKINS J
AUTHOR ADDRESS: DIV. CELL BIOL., JOHN CURTIN SCHOOL MEDICAL RES.,
AUSTRALIAN NATIONAL UNIV., P.O. BOX 334, CANBERRA, AUST.

JOURNAL: VIROLOGY 177 (2). 1990. 595-605.
FULL JOURNAL NAME: Virology
CODEN: VIRLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Infection of quiescent rat kidney cells with human adenovirus is shown to transcriptionally stimulate (transactivate) the p53 oncogene. The increased transcription results in an accumulation of p53-specific mRNA in parallel with an increase in p53 protein levels, although there is a considerable delay between trascriptional activation and the detection of stable p53 mRNA and protein. The induction of p53 is detectable with two monoclonal antibodies recognizing different epitopes. The induction of %%%p53%%% by %%%adenovirus%%% is delayed compared to
induction by serum, and it occurs after the onset of adenovirus-induced cellular DNA-replication. Thus, adenovirus-induced DNA replication bypasses a G0/G1 control point. Experiments with hydroxyurea show that p53 activation does not require continued cell cycling and thus is likely to be a direct consequence of viral gene expression. Finally, the induction of p53 is shown to be dependent on expression of the 289-residue product encoded by the viral E1a gene.

5/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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07297293 BIOSIS NO.: 000090077180
ASSOCIATION BETWEEN THE CELLULAR %%%P53%%% AND THE %%%ADENOVIRUS%%% 5
E1B-55KD PROTEINS REDUCES THE ONCOGENICITY OF AD-TRANSFORMED CELLS

AUTHOR: DEN HEUVEL S J L; VAN LAAR T; KAST W M; MELIEF C J M; ZANTEMA A;
VAN DER EB A J
AUTHOR ADDRESS: DEP. MED. BIOCHEM., SYLVIUS LAB., P.O. BOX 9503, 2300 RA
LEIDEN, THE NETHERLANDS CANCER INST., ANTONI LEEUWENHOEK HUIS,
PLESMANLAAN 121, 1066 CX AMSTERDAM, THE NETHERLANDS.

JOURNAL: EMBO (EUR MOL BIOL ORGAN) J 9 (8). 1990. 2621-2630.
FULL JOURNAL NAME: EMBO (European Molecular Biology Organization) Journal
CODEN: EMJOD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The association of the cellular p53 protein with the E1B-55kd protein of adenovirus 5 (Ad5) is thought to result in inactivation of the p53 recessive oncogene product. Here we show that Ad5 E1-transformed 3Y1 rat cells which express low levels of the 55 kd E1B protein do not contain the p53-E1B 55kd complex. These cells have nuclearly located p53 and are highly oncogenic in nude mice. In 3Y1 cells expressing the E1B protein at a sufficiently high level, association between p53 and E1B-55kd occurs, resulting in an almost complete trapping of p53 into a discrete cytoplasmic body. These cells only form tumors after a very long latency period and in the tumors that eventually appear selection has occurred in favor of cells lacking the complex and containing free nuclear p53. Comparable results were found when highly oncogenic Ad12-transformed cells were supertransfected with the Ad5 E1B region. In none of the Ad-transformed mouse, rat and human cell lines examined, could we detect p53, of abnormal molecular weight or association with hsc70, neither could we immunoprecipitate p53 by the mutant specific antibody PAb240. These data suggest that a high level of nuclear p53 with a wild-type conformation contributes to the oncogenicity of Ad transformed cells.

5/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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06690534 BIOSIS NO.: 000087132727
ABILITY OF %%%P53%%% AND THE %%%ADENOVIRUS%%% E1B 58-KILODALTON PROTEIN TO
FORM A COMPLEX IS DETERMINED BY P53

AUTHOR: BRAITHWAITE A W; JENKINS J R
AUTHOR ADDRESS: MARIE CURIE RES. INST., THE CHART, OXTED, SURREY RH8 OTL,
ENGLAND.

JOURNAL: J VIROL 63 (4). 1989. 1792-1799.
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have investigated p53-E1b 58-kilodalton (kDa) protein complex
formation during permissive semipermissive infections with adenovirus type 5 (Ad5) dl309. While metabolic labeling studies easily detected p53-E1b 58-kDa protein complexes in transformed rat cells (XhoI-C), the same methods have not revealed complexes during infection of either human osteosarcoma cells (permissive) or normal rat kidney cells (semipermissive). Complexes were not detectable at any stage during the replicative cycle of Ad5 dl309 in osteosarcoma cells, and they could not be stabilized by using an in vivo cross-linking agent. In addition, using the E4-defective mutant Ad5 dl355, no complexes were observed either. Thus, the lack of p53-E1b 58-kDa protein complex formation during infection is not due to competition from teh E4 34-kDa protein. In vitro association experiments showed that in vitro-translated mouse and human p53 could form complexes with E1b 58-kDa antigen expressed during infection. Thus, such E1b proteins are competent to form complexes. The converse experiment, in which in vitro-translated E1b 58-kDa protein was mixed with lysates of osteosarcoma cells, showed little or no p53-E1b 58-kDa protein association, even though the in vitro E1b 58-kDa protein could associate stably with p53 from cells containing endogenous p53-E1b 58-kDa protein complex. These data suggest that competence to form p53-E1b 58-kDa protein complexes resides in some property of p53.

5/3,AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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06215959 BIOSIS NO.: 000086050141
THE INTRACELLULAR DISTRIBUTION OF THE TRANSFORMATION-ASSOCIATED PROTEIN %%%P53%%% IN %%%ADENOVIRUS%%%-TRANSFORMED RODENT CELLS

AUTHOR: ZAJDEL M E B; BLAIR G E
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. LEEDS, LEEDS LS2 9JT, UK.

JOURNAL: ONCOGENE 2 (6). 1988. 579-584.
FULL JOURNAL NAME: Oncogene
CODEN: ONCNE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The intracellular distribution of the transformation-associated cellular protein p53 was studied by indirect immunofluorescence in a series of adenovirus-transformed rodent cells. In most adenovirus 2 or 5 (group C) transformed cell lines p53 was detected in discrete areas in nuclei and in all cell lines p53 was also present in a perinuclear structure. The adenovirus 2 or 5 E1B-58 kD protein, previously found to form molecular complexes with p53 in group C transformed cells, colocalized with p53 in both intracellular locations. Further studies on the region of the cell corresponding to the perinuclear body containing p53 showed that it frequently included the centrosomes of the transformed cell. The intranuclear p53 was released by mild DNase I digestion.

5/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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06149598 BIOSIS NO.: 000085112750
EXPRESSION OF THE CELLULAR %%%P53%%% PROTEIN IN CELLS TRANSFORMED BY
%%%ADENOVIRUS%%% 12 AND VIRAL DNA FRAGMENTS

AUTHOR: MAK I; MAK S; BENCHIMOL S
AUTHOR ADDRESS: BIOL. DEP., MCMASTER UNIV., HAMILTON, ONTARIO, CANADA L8S
4K1.

JOURNAL: VIROLOGY 163 (1). 1988. 201-204.
FULL JOURNAL NAME: Virology
CODEN: VIRLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Expression of the p53 cellular phosphoprotein was examined in rat
cells transformed by adenovirus 12 (Ad12) virions and by fragments of Ad12 DNA. p53 was detected in all the cell lines examined. Steady-state levels of p53 were highest in cells transformed by the entire E1 region rather than by E1A alone. Physical association between p53 and the Ad12 E1B 55K protein was not detected. The Ad12 E1B-encoded 55K protein, but not the Ad12 E1B 17K and 19K proteins, appears to participate in regulating p53 protein levels.

5/3,AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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05115708 BIOSIS NO.: 000081073832
TUMORIGENICITY OF FIBROBLAST LINES EXPRESSING THE ADENOVIRUS E-1A CELLULAR
P-53 OR NORMAL C-MYC GENES

AUTHOR: KELEKAR A; COLE M D
AUTHOR ADDRESS: DEP. MOLECULAR BIOL., PRINCETON UNIV., PRINCETON, N.J.
08544.

JOURNAL: MOL CELL BIOL 6 (1). 1986. 7-14.
FULL JOURNAL NAME: Molecular and Cellular Biology
CODEN: MCEBD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

QH506 .M6

ABSTRACT: Cellular and viral oncogenes have been linked to the transformation of established cell lines in vitro, to the induction of tumors in vivo, and to the partial transformation or immortalization of primary cells. Based on the ability to cooperate with mutated ras oncogenes in the transformation of primary cells, the %%%adenovirus%%% E1a and cellular %%%p53%%% genes have been assigned an immortalizing activity. It is demonstrated in this paper that the adenovirus type 5 E1a gene and simian virus 40 promotor-linked p53 cDNA are able to transform previously immortalized cells to a tumorigenic phenotype without a significant change in cell morphology. It is also shown that, when linked to a constitutive promoter, the normal mouse and human c-myc genes have the same transforming activity. Cells transformed by each of these oncogenes have an increased capacity to grow in the absence of growth factors and a limited anchorage-independent growth capability.

5/3,AB/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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04294564 BIOSIS NO.: 000078024106
ADENOVIRUS EARLY REGION 1B 58000 DALTON TUMOR ANTIGEN IS PHYSICALLY
ASSOCIATED WITH AN EARLY REGION 4 25000 DALTON PROTEIN IN PRODUCTIVELY
INFECTED CELLS

AUTHOR: SARNOW P; HEARING P; ANDERSON C W; HALBERT D N; SHENK T; LEVINE A J
AUTHOR ADDRESS: DEP. MICROBIOL., SCH. MED., STATE UNIV. N.Y. STONY BROOK,
STONY BROOK, N.Y. 11794.

JOURNAL: J VIROL 49 (3). 1984. 692-700.
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In soluble protein extracts obtained from adenovirus productive infected cells, monoclonal antibodies directed against the early region 1B 58,000-dalton (E1B-58K) protein immunoprecipitated, in addition to this protein, a polypeptide of 25,000 MW. An analysis of tryptic peptides derived from this 25K protein demonstrated that it was unrelated to the E1B-58K protein. The tryptic peptide maps of the 25K protein produced in adenovirus 5 (Ad5)-infected human cervical carcinoma HeLa cells and hamster kidney BHK cells were identical; Ad3-infected HeLa cells produced a different 25K protein. The viral origin of this 25K protein was confirmed by an amino acid sequence determination of 5 methionine residues in 2 Ad2 tryptic peptides derived from the 25K protein. The positions of these methionine residues in the 25K protein were compared with the nucleotide sequence of Ad2 and uniquely mapped the gene for this protein to early region 4, subregion 6 of the viral genome. A mutant of Ad5 was obtained (Ad5 dl342) which failed to produce detectable levels of the E1B-58K protein. In HeLa cells infected with this mutant, monoclonal antibodies directed against the E1B-58K protein failed to detect the associated 25K protein. In human embryonic kidney 293 cells infected with Ad5 dl342, which contain an E1B/58K protein encoded by the integrated adenovirus genome, the mutant produced an E4-25K protein which associated with the E1B-58K protein derived from the integrated genome. Extracts of labeled Ad5 dl342-infected HeLa cells or 293 cells (E1B-58K+). When the mixed extracts were incubated with the E1B-58K monoclonal antibody, a labeled E4-25K protein was coimmunoprecipitated. When extracts of Ad5 dl342-infected HeLa cells and uninfected HeLa cells (both E1B-58K-) were mixed, the E1B-58K monoclonal antibody failed to immunoselect the E4-25K protein. Evidently, the E1B-58K antigen is physically associated with an E4-25K protein in productively infected cells. This is the same E1B-58K protein that was previously shown to be associated with the cellular %%%p53%%% antigen in %%%adenovirus%%%-transformed cells.

5/3,AB/9 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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04336165 EMBASE No: 1990224228
Association between the cellular %%%p53%%% and the %%%adenovirus%%% 5
E1B-55kd proteins reduces the oncogenicity of Ad-transformed cells
Van Den Heuvel S.J.L.; Van Laar T.; Kast W.M.; Melief C.J.M.; Zantema A.; Van Der Eb A.J.
Sylvius Laboratories, Department of Medical Biochemistry, PO Box 9503, 2300 RA Leiden Netherlands
EMBO Journal (EMBO J.) (United Kingdom) 1990, 9/8 (2621-2629)

CODEN: EMJOD ISSN: 0261-4189
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The association of the cellular p53 protein with the E1B-55kd protein of adenovirus 5 (Ad5) is thought to result in inactivation of the p53 recessive oncogene product. Here we show that Ad5 E1-transformed 3Y1 rat cells which express low levels of the 55 kd E1B protein do not contain the p53-E1B 55kd complex. These cells have nuclearly located p53 and are highly oncogenic in nude mice. In 3Y1 cells expressing the E1B protein at a sufficiently high level, association between p53 and E1B-55kd occurs, resulting in an almost complete trapping of p53 into a discrete cytoplasmic body. These cells only form tumors after a very long latency period and in the tumors that eventually appear selection has occurred in favor of cells lacking the complex and containing free nuclear p53. Comparable results were found when highly oncogenic Ad12-transformed cells were supertransfected with the Ad5 E1B region. In none of the Ad-transformed mouse, rat and human cell lines examined, could we detect p53 of abnormal molecular weight or association with hsc70, neither could we immunoprecipitate p53 by the mutant specific antibody PAb240. These data suggest that a high level of nuclear p53 with a wild-type conformation contributes to the oncogenicity of Ad transformed cells.

5/3,AB/10 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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03707387 EMBASE No: 1988156823
The intracellular distribution of the transformation-associated protein %%%p53%%% in %%%adenovirus%%%-transformed rodent cells
Blair Zajdel M.E.; Blair G.E.
Department of Biochemistry, University of Leeds, Leeds LS2 9JT United Kingdom
Oncogene (ONCOGENE) (United Kingdom) 1988, 2/6 (579-584)

CODEN: ONCNE ISSN: 0950-9232
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The intracellular distribution of the transformation-associated cellular protein p53 was studied by indirect immunofluorescence in a series of adenovirus-transformed rodent cells. In most adenovirus 2 or 5 (group C) transformed cell lines p53 was detected in discrete areas in nuclei and in all cell lines p53 was also present in a perinuclear structure. The adenovirus 2 or 5 E1B-58 kD protein, previously found to form molecular complexes with p53 in group c transformed cells, colocalized with p53 in both intracellular locations. Further studies on the region of the cell corresponding to the perinuclear body containing p53 showed that it frequently included the centrosomes of the transformed cell. The intranuclear p53 was released by mild DNAase I digestion.

5/3,AB/11 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
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03238562 EMBASE No: 1986081139
Tumorigenicity of fibroblast lines expressing the %%%adenovirus%%% E1a, cellular %%%p53%%%, or normal c-myc genes
Kelekar A.; Cole M.D.
Department of Molecular Biology, Princeton University, Princeton, NJ 08544 United States
Molecular and Cellular Biology (MOL. CELL. BIOL.) (United States) 1986, 6/1 (7-14)

CODEN: MCEBD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Cellular and viral oncogenes have been linked to the transformation of established cell lines in vitro, to the induction of tumors in vivo, and to the partial transformation or immortalization of primary cells. Based on the ability to cooperate with mutated ras oncogenes in the transformation of primary cells, the %%%adenovirus%%% E1a and cellular %%%p53%%% genes
have been assigned an immortalizing activity. It is demonstrated in this paper that the adenovirus type 5 E1a gene and simian virus 40 promotor-linked p53 cDNA are able to transform previously immortalized cells to a tumorigenic phenotype without a significant change in cell morphology. It is also shown that, when linked to a constitutive promotor, the normal mouse and human c-myc genes have the same transforming activity. Cells transformed by each of these oncogenes have an increase capacity to grow in the absence of growth factors and a limited anchorage-independent growth capability.

5/3,AB/12 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
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02148051 EMBASE No: 1982127167
The regulation of a cellular protein, p53, in transformed cells and its association with viral tumor antigens
Levine A.J.; Kaplan L.; Oren M.; et al.
State Univ. New York, Stony Brook, NY United States
Hepatology (HEPATOLOGY) (United States) 1982, 2/2 Suppl. (58S-60S)

CODEN: HPTLD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

p53 is a cellular protein detected in elevated levels in a large number of transformed cells. High levels of p53 have been measured in cells transformed by DNA and RNA viruses, chemical carcinogens, X-irradiation, naturally occurring tumors, or spontaneously transformed cell lines. The protein is conserved over evolutionary time scales with an homologous p53 detected in mouse, rat, hamster, rabbit, monkey, or human cells. In the case of the DNA tumor virus, e.g., SV40, %%%adenovirus%%%, and Epstein-Barr
virus, %%%p53%%% is associated in a physical complex with one of the viral tumor antigens. Employing monoclonal antibodies directed against p53, the

viral tumor antigens from cells transformed by these viruses are coimmunoprecipitated by virtue of their association with p53. This approach should permit the detection of viral or cellular tumor antigens associated with p53 from tumors with suspected viral etiologies.

5/3,AB/13 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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115045663 CA: 115(5)45663c PATENT
Methods and kits for detection of loss of the wild-type p53 gene for cancer diagnosis and method of supplying the gene for treatment
INVENTOR(AUTHOR): Vogelstein, Bert; Baker, Suzanne J.; Fearon, Eric R.;
Nigro, Janice M.
LOCATION: USA
ASSIGNEE: Johns Hopkins University
PATENT: European Pat. Appl. ; EP 390323 A2 DATE: 901003
APPLICATION: EP 90301817 (900220) *US 330566 (890329)
PAGES: 17 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C12Q-001/68A;
C07H-021/04B; C12N-015/00 DESIGNATED COUNTRIES: CH; DE; FR; GB; IT; LI; NL

5/3,AB/14 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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106065141 CA: 106(9)65141y JOURNAL
Altered regulation of c-myc expression in adenovirus-transformed cells
AUTHOR(S): Braithwaite, Antony W.; Fry, Kathy E.; LeJeune, Sue; Naora, Hiroto
LOCATION: Res. Sch. Biol. Sci., Aust. Natl. Univ., Canberra, Australia
JOURNAL: Can. J. Genet. Cytol. DATE: 1986 VOLUME: 28 NUMBER: 5
PAGES: 712-24 CODEN: CNJGA8 ISSN: 0008-4093 LANGUAGE: English

5/3,AB/15 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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105040309 CA: 105(5)40309a JOURNAL
Modulation of the level of expression of cellular genes in adenovirus 12-infected and transformed human cells
AUTHOR(S): Grand, Roger J. A.; Gallimore, Phillip H.
LOCATION: Med. Sch., Univ. Birmingham, Birmingham, UK, B15 2TJ
JOURNAL: EMBO J. DATE: 1986 VOLUME: 5 NUMBER: 6 PAGES: 1253-60
CODEN: EMJODG ISSN: 0261-4189 LANGUAGE: English

5/3,AB/16 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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103210586 CA: 103(25)210586s JOURNAL
Adenovirus serotype determines association and localization of the large E1B tumor antigen with cellular tumor antigen p53 in transformed cells
AUTHOR(S): Zantema, Alt; Schrier, Peter I.; Davis-Olivier, Arja; Van Laar, Theo; Vaessen, Ruud T. M. J.; Van der Eb, Alex J.
LOCATION: Dep. Med. Biochem., Univ. Leiden, 2333 AL, Leiden, Neth.
JOURNAL: Mol. Cell. Biol. DATE: 1985 VOLUME: 5 NUMBER: 11 PAGES:
3084-91 CODEN: MCEBD4 ISSN: 0270-7306 LANGUAGE: English
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